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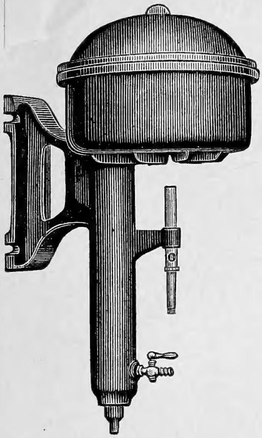

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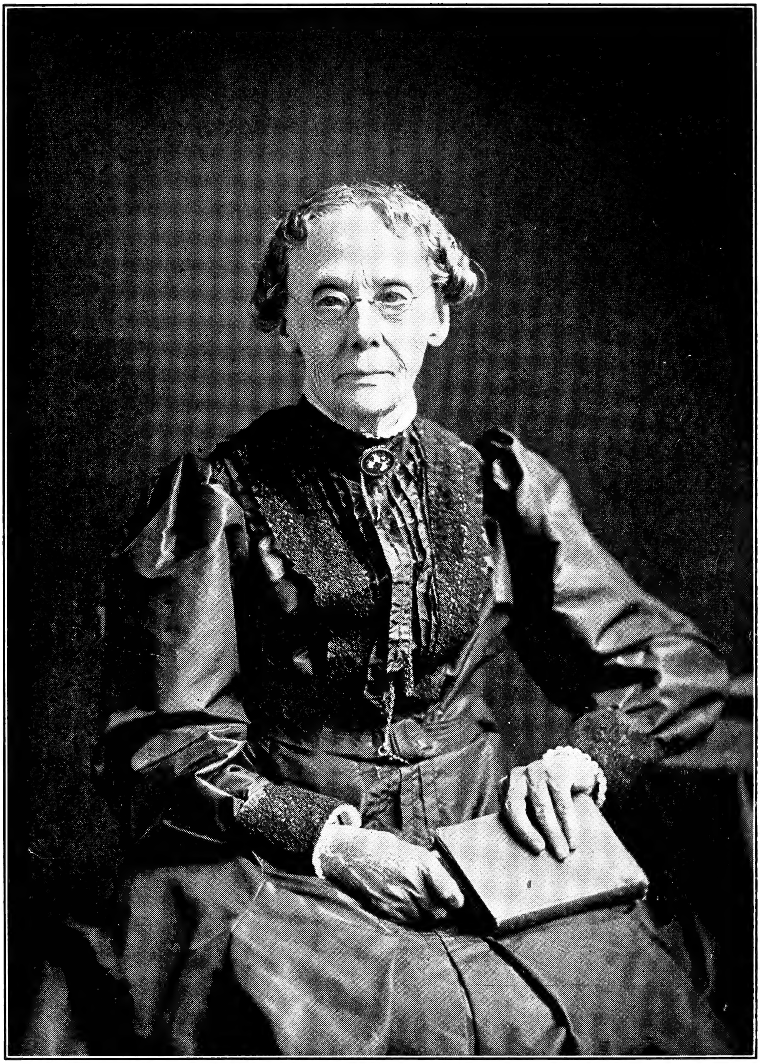

DR. SUSAN HAYHURST, 1820–1909.

THE AMERICAN
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JANUARY, 1911

THE CONSTITUENTS OF THE RHIZOME OF IRIS VERSICOLOR.

By Frederick B. Power and Arthur H. Salway.

A Contribution from the Wellcome Chemical Research Laboratories, London.

The rhizome and roots of *Iris versicolor,* Linné (Nat. ord. *Iridaceæ*), commonly known as the "Larger Blue Flag," were recognized for several decades by the Pharmacopœia of the United States (Revisions of 1870, 1880 and 1890) under the official title of *Iris,* together with liquid and solid extracts prepared therefrom. In the eighth revision (1900), however, of the above-mentioned work the drug was deleted, probably on account of its limited use or the variability and uncertainty of its action. Under the names of "Irisin" or "Iridin" preparations have been introduced, and are still somewhat employed medicinally, which consist either of the resin or of an ethereal or alcoholic extract of the drug.

Although in the literature [1] it has been recorded that the rhizome of *Iris versicolor* contains starch, gum, tannin, sugar, an acid resin, and fatty oil, together with some volatile matter and possibly an alkaloid, its constituents have never been thoroughly investigated. As the rhizome, at least in the fresh state, evidently possesses considerable potency, acting as a cathartic and emetic, although its medicinal activity is stated to become impaired by age, it was deemed desirable to subject it to a complete chemical examination.

EXPERIMENTAL.

The material employed for the present investigation consisted of commercial "Blue Flag Root," the identity of which was established, and it appeared to be of good quality.

As a preliminary experiment, a small portion of the ground

[1] This *Journal,* 1876, **48**, p. 406; 1881, **53**, p. 601; 1884, **56**, p. 616.

material was tested for the presence of an alkaloid, but with a negative result. A further quantity (25 grammes) of the ground material was successively extracted in a Soxhlet apparatus with various solvents, when the following amounts of extract, dried at 100°, were obtained:

Petroleum (b. p. 35–50°)	extracted	0.30 Gm.	=	1.2 per cent.
Ether	"	0.80 "	=	3.2 " "
Chloroform	"	0.22 "	=	0.9 " "
Ethyl acetate	"	0.42 "	=	1.7 " "
Alcohol	"	4.13 "	=	16.5 " "
	Total	5.87 Gm.	=	23.5 per cent.

For the purpose of a complete examination 62.82 kilogrammes of the ground material were extracted by continuous percolation with hot alcohol. After removing the greater portion of the alcohol, there remained a viscid, dark-colored extract, amounting to 15.72 kilogrammes.

Distillation of the Extract with Steam. Separation of an Essential Oil.

Two kilogrammes of the above-mentioned alcoholic extract were mixed with a little water, and subjected to distillation in a current of steam for several hours. The distillate contained a small quantity of oil floating on the surface, which was extracted with ether. The ethereal liquid was dried, and the solvent removed, when there remained 2 grammes of an *essential oil,* this amount corresponding to 0.025 per cent. of the weight of the drug. The essential oil possessed a yellow color, a strong, somewhat unpleasant odor, and contained traces of furfuraldehyde, as indicated by the aniline color test. Its density was 0.9410 at 20°/20°; when examined polarimetrically, no appreciable optical rotation could be observed.

Non-volatile Constituents of the Extract.

After removal of the essential oil, as above described, there remained in the distillation flask a deep brown, aqueous liquid (A) and a brown resin (B). These were separated by filtration, and the resin well washed with water, the washings being added to the main portion of the aqueous liquid.

Examination of the Aqueous Liquid (A).

The aqueous liquid was concentrated to a convenient volume under diminished pressure, and then repeatedly extracted with ether, the ethereal extracts being united, washed with a little water, and dried with anhydrous sodium sulphate. On removing the solvent, 15 grammes of an oily residue were obtained, which did not solidify on keeping. For the further examination of this product it was redissolved in ether, and the ethereal liquid shaken successively with solutions of ammonium carbonate (*a*), sodium carbonate (*b*), and sodium hydroxide (*c*).

Isolation of iso*Phthalic Acid,* $C_6H_4(CO_2H)_2$.

The ammonium carbonate extract (*a*) of the above-mentioned, ethereal liquid was acidified with dilute sulphuric acid, when an oil was precipitated which was taken up by ether. This ethereal solution was then washed, dried, and the solvent removed, when 10.5 grammes of a brown, viscid oil remained. The latter was next heated with methyl alcohol in a current of dry hydrochloric acid gas, and thus converted into its methyl ester, which, by treatment with dilute, aqueous sodium hydroxide could be separated into phenolic and non-phenolic portions. The portion insoluble in alkali, comprising the non-phenolic esters, amounted to 7 grammes. It distilled at 140–260°/20 mm., the greater portion, however, passing over at 150–180°/20 mm. This ester was then converted into the corresponding acid by heating for a short time with alcoholic potassium hydroxide. After hydrolysis was complete, the alcohol was removed, and the alkaline liquid acidified with dilute sulphuric acid, when a semi-solid, oily product was precipitated. The latter was removed by filtration, dried on a porous tile, and purified by crystallization from dilute alcohol. It was thus obtained in colorless, glistening leaflets, which did not melt below 300°.

0.0919 required for neutralization 10.85 c.c. $\frac{N}{10}$ $Ba(OH)_2$.
Neutralization value = 66.2
$C_6H_4(CO_2H)_2$ requires Neutralization value = 66.8

The crystalline acid, above described, was only sparingly soluble in hot water, but readily soluble in alcohol. When heated strongly in an ignition tube, it sublimed, forming colorless prisms on the cooler portions of the tube. Its barium salt was readily soluble in

water. These properties, together with the result of its titration, as given above, indicated it to be *iso*phthalic acid. In order to confirm its identity, a portion of the substance was heated with phosphorus pentachloride in the presence of benzene, and the product vigorously agitated with concentrated ammonia. In this manner an acid amide was formed, which was collected and well washed with water. The latter compound sintered at 260° and melted completely at 275°. A known specimen of *iso*phthalic acid, when similarly treated, also yielded an acid amide sintering at 260° and melting at 275°, and when the two specimens of amide were mixed the melting point remained unaltered.

The above-described substance was thus identified as *iso*phthalic acid, the occurrence of which in nature does not appear to have been hitherto observed. The amount of this acid obtained from 2 kilogrammes of the alcoholic extract of "Blue Flag Root" was about 0.15 gramme, thus corresponding to 0.0019 per cent. of the weight of the drug.

The phenolic methyl esters, which had been separated from the non-phenolic portion by means of sodium hydroxide, as above described, were hydrolyzed by heating for a short time with an aqueous solution of this alkali. The liquid was then acidified, when a resinous precipitate was deposited, which was extracted with ether. The ethereal liquid was washed and dried, and, on removing the solvent, yielded about 1 gramme of a brown oil. Since the latter did not show any indication of crystallizing, it was agitated with light petroleum, the petroleum extract decanted from insoluble oil, and the solvent allowed to evaporate. A trace of a crystalline solid was thus obtained, which gave a violet coloration with ferric chloride as well as the characteristic odor of oil of wintergreen when heated with methyl alcohol and a few drops of concentrated sulphuric acid. The presence of salicylic acid was thus indicated, but the amount was too small to admit of complete identification. That portion of the oil which was insoluble in light petroleum was again converted into its methyl ester, and the latter benzoylated by the Schotten-Baumann method. The product was oily, but gradually deposited a few colorless crystals. These were separated from adhering oil by spreading them on a porous tile, and then recrystallized from alcohol, when they separated in stellar aggregates of fine needles, melting

at 110°. The amount of this substance was too small for further examination.

The sodium carbonate (*b*) and the sodium hydroxide (*c*) extracts of the original ethereal liquid, when acidified, yielded only small quantities of gummy substances from which no definite compound could be isolated. On finally evaporating the ethereal liquids, which had thus been completely extracted with alkalies, 1.5 grammes of a yellow, amorphous mass remained.

The original aqueous liquid (A), which had been extracted with ether as above described, was next repeatedly shaken with amyl alcohol. The united amyl alcoholic extracts were washed with water, and then extracted successively with aqueous solutions of ammonium carbonate, sodium carbonate, and sodium hydroxide. The ammonium carbonate extract, when acidified with dilute sulphuric acid, yielded a resinous precipitate, which was taken up by amyl alcohol, the solution being washed, dried, and the solvent removed. The brown syrup thus obtained, which showed no tendency to crystallize, gave an intense black coloration with ferric chloride, and evidently contained tannin. For the further examination of this syrup it was esterified, but no definite substance could be isolated by this treatment.

The sodium carbonate and sodium hydroxide extracts of the amyl alcoholic liquid yielded only small quantities of brown, amorphous resins, which were specially examined for glucosides, but no positive evidence of the presence of such compounds was afforded. The amyl alcoholic liquid, which had been extracted with the various alkalies, was finally washed, and the solvent removed under diminished pressure. A thick, gummy mass, amounting to about 2 grammes, was thus obtained, but no crystalline compound could be isolated from it.

The aqueous liquid which had been extracted with ether and with amyl alcohol, as above described, was dark brown in color, and gave a copious brown precipitate on the addition of a slight excess of basic lead acetate. The lead precipitate was collected, thoroughly washed, then suspended in water, and decomposed by hydrogen sulphide. After removing the lead sulphide by filtration, the filtrate was concentrated under diminished pressure to a small volume. The concentrated liquid was light yellow, gave a faint brown coloration with ferric chloride, and, after standing for some

time, deposited a brown, amorphous solid, but nothing crystalline was obtained from it.

The filtrate from the basic lead acetate precipitate, after removal of the excess of lead, gave a slight precipitate with potassium mercuric iodide, and when heated with potassium hydroxide a strong ammoniacal odor was developed, thus indicating the probable presence of soluble protein products. It readily reduced Fehling's solution, and contained a large amount of sugar, which yielded *d*-phenylglucosazone, melting and decomposing at 212°. It also contained some potassium salts, since the addition of an aqueous solution of picric acid to a portion of the liquid caused a gradual separation of crystals of potassium picrate. The main portion of the aqueous liquid was concentrated to the consistency of a syrup and kept for a considerable time, but nothing crystalline was deposited.

The Resins (B).

The resinous material which had been separated from the original alcoholic extract, as previously described, was a dark-colored, soft solid, and amounted to 694 grammes, thus representing about 8.7 per cent. of the weight of the drug. It was digested with hot alcohol, the liquid brought on to purified sawdust, and the thoroughly dried mixture then extracted successively in a large Soxhlet apparatus with various solvents. The amounts of the respective extracts, dried at 100°, were as follows:

Petroleum (b. p. 35–50°)	extracted	296.0	Gms.	= 42.6	per	cent.
Ether	"	226.0	"	= 32.6	"	"
Chloroform	"	38.2	"	= 5.5	"	"
Ethyl acetate	"	16.4	"	= 2.4	"	"
Alcohol	"	30.2	"	= 4.4	"	"
	Total	606.8	Gms.	= 87.5	per	cent.

From these results it would appear that a portion of the resin had been rendered insoluble during the process of extraction.

Petroleum Extract of the Resin.

The petroleum extract of the resin consisted of a dark-colored, oily product, and amounted to 296 grammes. It was dissolved in a large volume of ether, and the ethereal liquid shaken with aqueous

ammonium carbonate, which, however, removed only traces of gummy matter. An attempt subsequently to extract the ethereal liquid with aqueous sodium hydroxide resulted in the formation of an emulsion, which did not separate after several days. The ether was therefore completely removed from the mixture, and the residue hydrolyzed by heating for an hour with an excess of alcoholic potassium hydroxide. After removing the greater portion of the alcohol, water was added, and the alkaline mixture shaken repeatedly with ether. These ethereal extracts were united, washed, dried, and the solvent removed, when a yellowish-brown, semi-solid mass was obtained. This amounted to 35 grammes, and represented the unsaponifiable portion of the petroleum extract of the resin.

Isolation of a Phytosterol, $C_{27}H_{46}O$, *Myricyl Alcohol,* $C_{31}H_{64}O$, *and Heptacosane,* $C_{27}H_{56}$.

The above-described, brown, semi-solid mass was dissolved in a mixture of alcohol and ethyl acetate, and subjected to a process of fractional crystallization. The more soluble fraction ultimately yielded a crystalline substance, which separated from alcohol in colorless needles. This substance, when air-dried, melted at 133°, but, when dried at 100°, it lost water of crystallization, and then melted at 148°.

0.1714, when heated at 110°, lost 0.0076 H_2O. $H_2O = 4.4$

0.1052, dried at 110°, gave 0.3236 CO_2 and 0.1144 H_2O.

$C = 83.9$; $H = 12.1$

$C_{27}H_{46}O,H_2O$ requires $H_2O = 4.5$ per cent.

$C_{27}H_{46}O$ requires $C = 83.9$; $H = 11.9$ per cent.

The above-described substance has thus been shown to agree in composition with a phytosterol of the formula $C_{27}H_{46}O$, and it yielded the color reactions of that class of compounds. Its optical rotatory power was determined with the following result:

0.1638 of anhydrous substance, made up to 25 c.c. with chloroform, gave $a_D - 0° 28'$ in a 2 dcm. tube, whence $[a]_D - 35.6°$.

The more sparingly soluble crystalline deposits obtained by the above-mentioned fractionation melted indefinitely over a considerable range of temperature, namely from 63 to 77°, and apparently consisted of a mixture of a hydrocarbon and a fatty alcohol. They were therefore heated for an hour at 130° with an equal weight of phthalic anhydride in the presence of xylene. The product of the reaction was then dissolved in a mixture of ether and chloroform,

and the solution shaken with aqueous sodium carbonate, when the sodium salt of an acid phthalic ester was immediately deposited. The latter was collected, and washed with a mixture of ether and chloroform, and then hydrolyzed by heating with alcoholic sodium hydroxide. After removing the alcohol from the reaction product, water was added, and the fatty alcohol thus precipitated was collected and crystallized from ethyl acetate, when minute, colorless needles, melting at 84°, were obtained. This substance was analyzed with the following result:

0.0913 gave 0.2742 CO_2 and 0.1154 H_2O. C = 81.9; H = 14.1

$C_{31}H_{64}O$ requires C = 82.3; H = 14.2 per cent.

The compound was thus identified as myricyl alcohol.

The ethyl acetate mother-liquors, remaining after the separation of the myricyl alcohol, yielded a small quantity of a crystalline substance melting at 77–78°. The melting point of this compound, together with the method of its isolation, would indicate that it consisted of ceryl alcohol, but the amount of substance was too small for an analysis.

The ether-chloroform solution which had been shaken with aqueous sodium carbonate to remove the myricyl acid phthalate, as above described, was evaporated, and the residue heated with alcoholic sodium hydroxide to remove the excess of phthalic anhydride. After evaporating the alcohol, and adding water to the residue, a small quantity of a solid was obtained, which was collected and recrystallized from ethyl acetate. It separated from this solvent in small, colorless leaflets, melting at 64–66°.

0.0931 gave 0.2903 CO_2 and 0.1230 H_2O. C = 85.0; H = 14.7

$C_{27}H_{56}$ requires C = 85.3; H = 14.7 per cent.

It is evident from the analysis and the melting point determination of this substance that it was heptacosane.

Isolation of Ipuranol, $C_{23}H_{38}O_2(OH)_2$.

The alkaline liquid obtained by the hydrolysis of the petroleum extract of the resin, having been extracted with ether to remove unsaponifiable material, as above described, was next acidified with dilute sulphuric acid, when the fatty acids were precipitated as a dark-colored oil. The mixture was then shaken with ether, which dissolved the fatty acids, leaving, however, a small quantity (0.7 gramme) of a green solid undissolved. The latter was collected, washed with hot alcohol, and recrystallized from pyridine containing

a little alcohol. It separated from this solvent in stellar aggregates of small, colorless needles, which decomposed at 285–295°.

0.0648 gave 0.1718 CO_2 and 0.0600 H_2O. $C = 72.3$; $H = 10.3$

$C_{23}H_{40}O_4$ requires $C = 72.6$; $H = 10.5$ per cent.

This compound, when dissolved in chloroform with a little acetic anhydride, and a drop of concentrated sulphuric acid subsequently added, gave a transient pink coloration, rapidly changing to blue and green. It yielded an acetyl derivative, which crystallized in colorless leaflets melting at 162–163°, and when this was mixed with a known specimen of diacetylipuranol the melting point remained unaltered.

The above-described compound was thus definitely identified as ipuranol (compare this *Journal,* 1908, **80**, pp. 264, 576; *Journ. Chem. Soc.,* 1908, **93**, p. 907; 1909, **95**, p. 249; 1910, **97**, pp. 7, 1102; *Pharm. Journ.,* 1910, **84**, p. 327).

Examination of the Fatty Acids.

The ethereal solution of fatty acids, from which the ipuranol had been separated, was washed with water, dried with anhydrous sodium sulphate, and the solvent removed. The residue, amounting to about 210 grammes, was dissolved in absolute ethyl alcohol, and esterified by passing a current of dry hydrochloric acid gas into the boiling solution. The excess of alcohol was then evaporated, the residual oil taken up by ether, and the ethereal solution washed, first with aqueous sodium hydroxide, which extracted a quantity of resinous substance, and then with water until free from alkali. After drying the solution, and removing the ether, the residual ethyl ester was fractionally distilled under diminished pressure, when 5 fractions were ultimately obtained, possessing the following constants:

Fraction	B. p.	Saponification Value	Iodine Value
1.	140–155°/20mm.	249	2.5
2.	155–175°/20mm.	242	4.7
3.	175–195°/20mm.	224	15.3
4.	195–225°/20mm.	189	51.7
5.	above 225°/20mm.	...	...

Fraction 1.—This fraction, amounting to 12 grammes, distilled under atmospheric pressure at 260–270°. It possessed a fruity odor, and, from a consideration of its boiling point and saponification

value, appeared to consist chiefly of ethyl laurate (b. p. 269° ; saponification value 246). In order to confirm the presence of lauric acid, the entire fraction was hydrolyzed with alcoholic potassium hydroxide, and the mixture then acidified and distilled in a current of steam. A quantity of volatile fatty acid was thus obtained, which melted at 40°, and was further identified as lauric acid by means of its neutralization value.

0.3150 required for neutralization 15.7 c.c. $\frac{N}{10}$ $Ba(OH)_2$.
Neutralization value = 280.
$C_{12}H_{24}O_2$ requires Neutralization value = 280.

Fractions 2 and 3.—These fractions, which were small in amount, were united and hydrolyzed with alcoholic potassium hydroxide, in order to obtain the free fatty acids. The latter were then dissolved in hot alcohol, and separated into four different fractions by the successive addition of small quantities of concentrated aqueous barium acetate. These fractions of barium salt yielded acids which melted at 33–35°, 33–35°, 35–36°, and 39°, and whose neutralization values were 260, 261, 268, and 275 respectively. It was evident from these results that fractions 2 and 3 consisted of a mixture of lauric acid (neutralization value = 280) and the acids of higher carbon content contained in the succeeding fraction.

Fraction 4.—This fraction contained the greater portion of the total fatty acids, and amounted to 120 grammes. Its iodine value (51.7) indicated the presence of a considerable quantity of unsaturated acid. For its further examination the acids were regenerated by hydrolysis, and then fractionally precipitated in hot alcoholic solution with small portions of concentrated aqueous barium acetate. In this manner the saturated acids were precipitated in the first 4 fractions, while the final fraction, which was oily, contained the unsaturated acids, and was therefore put aside for subsequent examination, as described below. The barium salts of the saturated acids thus obtained were treated separately with dilute hydrochloric acid, and the liberated fatty acids recrystallized from alcohol. The several fractions were then found to melt at 54–56°, 54–56°, 54–55°, and 53–55° respectively, while the corresponding neutralization values were 209, 212.5, 216, and 217. It was evident from these results that the saturated acids contained in fraction 4 consisted of a mixture of stearic and palmitic acids, whose neutralization values are 198 and 219 respectively.

The unsaturated acids, which were regenerated from the abovementioned oily barium salt, still contained small quantities of saturated acids. The mixture was therefore converted into its lead salt, and the latter treated with cold ether. The portion insoluble in ether was found upon examination to consist of the lead salts of lauric and palmitic acids. The portion soluble in ether, when treated with dilute hydrochloric acid, yielded the unsaturated acids as a pale yellow oil, which possessed the following constants: neutralization value = 208; iodine value = 111.

In order to ascertain the constituents of the unsaturated acids, 12 grammes of the mixture were oxidized with dilute alkaline permanganate, as described by Lewkowitsch (*Chemical Technology and Analysis of Oils, Fats, and Waxes,* 1904, vol. i, p. 360), when the chief oxidation product was dihydroxystearic acid, melting at 128°.

0.3412 required for neutralization 10.95 c.c. $\frac{N}{10}$ KOH.

Neutralization value = 180.

$C_{18}H_{36}O_4$ requires Neutralization value = 178.

A small quantity of tetrahydroxystearic acid (sativic acid), melting at 156°, was also isolated.

0.3164 required for neutralization 9.1 c.c. $\frac{N}{10}$ KOH.

Neutralization value = 164.

$C_{18}H_{36}O_6$ requires Neutralization value = 164.

No linusic or *iso*linusic acid was present in the product of oxidation, and it may therefore be concluded that the unsaturated acids consisted of a mixture of oleic and linolic acids, the former predominating.

Isolation of Cerotic Acid, $C_{26}H_{52}O_2$.

Fraction 5.—The final fraction obtained by the distillation of the esters of the total fatty acids solidified in the receiver as a colorless solid. It was recrystallized several times from alcohol, when it separated in glistening leaflets, melting at 55–56°. This ester was then hydrolyzed, and the liberated fatty acid recrystallized from ethyl acetate. It was deposited from this solvent in colorless leaflets, melting at 78°, and was identified as cerotic acid.

0.1110 gave 0.3185 CO_2 and 0.1295 H_2O. C = 78.3; H = 13.0

0.1822 required for neutralization 4.75 c.c. $\frac{N}{10}$ KOH.

Neutralization value = 146.

$C_{26}H_{52}O_2$ requires C = 78.8; H = 13.1 per cent. Neutralization value = 142.

Ethereal Extract of the Resin.

This was a hard, black, brittle mass, and amounted to 226 grammes. It was digested with a large volume of ether, when a small portion of the resin (2 grammes) was found to be sparingly soluble in that solvent. The ethereal liquid was therefore filtered, and the undissolved portion separately examined. It was found to consist of ipuranol, $C_{23}H_{40}O_4$, which was identified by means of its diacetyl derivative, melting at 161–162°. This substance had already been isolated from the petroleum extract of the resin.

The ethereal liquid, from which the ipuranol had been removed by filtration, was then successively extracted with aqueous solutions of ammonium carbonate, sodium carbonate, and sodium hydroxide respectively. The ammonium carbonate and sodium carbonate solutions extracted only small quantities of amorphous, brown resins, from which no definite compound was isolated. The aqueous sodium hydroxide, on the other hand, extracted practically the whole of the resin as a thick, black liquid, a small quantity of the alkali being sufficient to extract a comparatively large amount of the resin, thus indicating that the latter possesses a very high molecular weight. On acidifying the alkaline extract, a brown, amorphous solid was precipitated, which was readily soluble in ether and alcohol. All attempts to isolate a crystalline compound from it were, however, unsuccessful. In order to ascertain whether the resin was glucosidic in character, a portion of it was heated for some time in alcoholic solution with dilute aqueous sulphuric acid. On removing the alcohol in a current of steam a quantity of resinous matter separated, which was collected and examined, but it yielded nothing crystalline. The aqueous liquid, after being freed from sulphuric acid by means of baryta was concentrated and tested for the presence of sugar, but with a negative result. The portion of resin extracted by ether is therefore non-glucosidic.

The ethereal liquid which had been shaken with alkalies, as above described, was washed, dried, and the solvent removed, when a small quantity of a thick oil was obtained. This was found to be similar in character to the petroleum extract of the resin, which had already been exhaustively examined.

Chloroform, Ethyl Acetate, and Alcohol Extracts of the Resin.

These were all black, brittle resins, and were small in amount. They were each carefully examined, but nothing of a crystalline

character could be isolated from them. Both the ethyl acetate and alcohol extracts of the resin were specially tested for the presence of a glucoside, but with a negative result.

SUMMARY AND PHYSIOLOGICAL TESTS.

The results of the present investigation of "Blue Flag Root" (the rhizome and roots of *Iris versicolor*, Linné), together with some physiological tests and the deductions therefrom, may be summarized as follows:

The material employed was the commercial drug, the genuineness of which was established, and it appeared to be of good quality. A preliminary test with a small portion of the material showed the absence of an alkaloid, and in the course of the investigation no evidence was obtained of the presence of a glucoside.

An alcoholic extract of the ground material, when distilled with steam, yielded a small amount of an essential oil, which possessed a yellow color, a strong, rather unpleasant odor, and had a density of 0.9410 at 20°/20°.

The portion of the extract which was soluble in water contained a little *iso*phthalic acid, $C_6H_4(CO_2H)_2$, which has not previously been observed to occur in nature, and apparently a trace of salicylic acid, together with tannin, and a sugar which yielded *d*-phenylglucosazone (m. p. 212°).

The portion of the extract which was insoluble in water consisted chiefly of a dark colored, soft resin, amounting to about 8.7 per cent. of the weight of the drug. From this resin the following definite products were isolated: A phytosterol, $C_{27}H_{46}O,H_2O$ (m. p. when anhydrous, 148°; $[a]_D$ —35.6°); myricyl alcohol, $C_{31}H_{64}O$; heptacosane, $C_{27}H_{56}$; ipuranol, $C_{23}H_{38}O_2(OH)_2$; and a mixture of fatty acids, consisting of lauric, palmitic, stearic, cerotic, oleic, and linolic acids.

As no definite substance had been isolated in the course of this investigation to which the reputed properties of "Blue Flag Root" could be attributed, the following crude products therefrom were kindly tested for us by Dr. H. H. Dale, Director of the Wellcome Physiological Research Laboratories, to whom we desire here to express our thanks:

I. The total alcoholic extract.

II. The total resinous material.

III. The portion of the alcoholic extract which was soluble in water.

IV. An aqueous extract of the drug, prepared without heat.

Each of these preparations was given to a dog by the mouth, Nos. I and II in amounts of 1 gramme, and III and IV in considerable quantity. No vomiting or modification of the fæces was produced, nor could any other sign of activity be detected.

Although the potency of "Blue Flag Root," in the fresh state, is evidently well established, it has also been recorded that its medicinal activity is impaired by age. From the results of the above experiments, it would appear that it is possible for the drug completely to lose its physiological activity.

A NOTE ON THE ASSAY OF LACTIC ACID.

By Elias Elvove.

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It has been pointed out by Murray[1] that the assay requirement of the U. S. Pharmacopœia in the case of lactic acid (75 per cent.) is out of harmony with its specific gravity requirement since a mixture of 75 per cent. lactic acid and 25 per cent. water has a specific gravity of about 1.175 at 25° C., whereas the U.S.P. specific gravity requirement ("about 1.206 at 25° C.") would correspond to a mixture of 85 to 88 per cent. lactic acid and 12 to 15 per cent. water. It occurred to the writer that this discrepancy might possibly be due to a weak point in the assay method which may cause the acid to appear weaker than it actually is. This further suggested the desirability of avoiding, if possible, the titration of the acid at a boiling temperature as called for by the present U.S.P., since the titration at a boiling temperature instead of at ordinary temperature involves not only comparative inconvenience but is also more liable to yield different results in the hands of different operators.

A consideration of the circumstances of this case appears to show that it is possible to avoid carrying out the titration at a boiling temperature. For it is quite probable that the object of the boiling is to reconvert into acid any lactone anhydride which may be present. And since it is known[2] that lactones in general do not take up water by mere boiling or are only partially converted into acid by such treatment, but are converted into salts of the corresponding

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[1] *Merck's Report,* N. Y., **16**, 248 (1907).

[2] Watts' Dictionary of Chemistry, vol. iii, p. 114 (1901).

acids by boiling with aqueous solutions of alkalies, it would seem that a much better plan for recovering the acid value of such anhydrides is to boil with a measured excess of a standard solution of alkali and determine the amount of alkali which remains uncombined by titration (at ordinary temperature) with a standard solution of acid. On looking into the matter, it was found that in the French Pharmacopœia (1908) such a plan has actually been adopted, the procedure consisting essentially in adding a measured excess of alkali, boiling for fifteen minutes, cooling, and then titrating the residual alkali. It was thought desirable, therefore, to obtain some comparative data concerning both this residual titration process and that in which the titration is carried out at a boiling temperature.

On titrating a dilute aqueous solution of lactic acid at a boiling temperature it was found that the result thus obtained may vary within comparatively wide limits, depending on what is taken as indicating the end-reaction, whether the coloring of the solution by the phenolphthalein indicator and its remaining on mixing the solution (first indication of neutrality), or whether the boiling is to be continued for some time after that point has been reached, and the length of time the boiling is continued after the first indication of neutrality. In the following work, therefore, two procedures were used in carrying out the titration at a boiling temperature. In one of these (designated as No. 2 in the Tables), the solution was first titrated to neutrality at ordinary temperature and the standard alkali then added in small portions (three drops) at a time and boiled after each such addition of the alkali until a decided pink color remained after the boiling had continued for one minute longer. The other procedure in which the titration was completed at a boiling temperature (designated as No. 3 in the Tables) was carried out in exactly the same way, but the titration was not considered ended until a decided pink color had remained after the boiling had been continued for ten minutes longer. Likewise, in the case of the residual titration after treatment with an excess of alkali, two procedures were used. In one of these (designated as No. 4 in the Tables), the stated amounts of the acid and alkali were well mixed and allowed to stand thirty minutes at ordinary temperature before titrating the excess alkali. In the other (designated as No. 5 in the Tables), the mixture was boiled for fifteen minutes, cooled, and the excess alkali then titrated with the standard acid. And in the latter case, in order to avoid any possibility of the alkali becoming

contaminated with the carbon dioxide which is given off by the flame of the burner, the boiling was effected in Erlenmeyer flasks which were fitted with india-rubber slit valves (Bunsen's valve). Eight samples of lactic acid were examined, the solution of each being also titrated directly at ordinary temperature (designated as procedure No. 1 in the Tables). Seven of these samples were obtained from American firms, while one was obtained from a German firm (Kahlbaum). The results obtained are given in the following tables:

TABLE I.

Showing Lactic Acid Strength of Various Commercial Samples of Lactic Acid as Determined by Various Procedures.

No. of sample.	No. of procedure	Amount of lactic acid solution taken.[3] (c.c.)	N/10 NaOH added before titration. (c.c.)	N/10 NaOH required. (c c.)	Lactic acid strength of sample.
1	1	20	0	19.05	72.14
1	2	20	0	21.90	82.94
1	3	20	0	22.60	85.59
1	4	20	40	23.15	87.67
1	5	20	40	23.15	87.67
2	1	20	0	18.30	71.95
2	2	20	0	21.10	82.95
2	3	20	0	21.90	86.10
2	4	20	40	22.45	88.26
2	5	20	40	22.55	88.65
3	1	20	0	18.05	71.86
3	2	20	0	21.00	83.63
3	3	20	0	21.60	85.99
3	4	20	40	22.40	89.18
3	5	20	40	22.40	89.18
4	1	20	0	18.40	71.72
4	2	20	0	21.25	82.83
4	3	20	0	22.00	85.75
4	4	20	40	22.60	88.10
4	5	20	40	22.70	88.48

[3] The solutions of lactic acid used contained the following amounts in grammes of the respective samples of lactic acid in 1000 c.c. of the solution: No. 1, 11.8825; No. 2, 11.4463; No. 3, 11.3034; No. 4, 11.5446; No. 5, 11.7030; No. 6, 11.6975; No. 7, 11.5736; No. 8, 11.5892.

TABLE I.—*Continued.*

No. of sample.	No. of procedure	Amount of lactic acid solution taken.[3] (c.c.)	N/10 NaOH added before titration. (c.c.)	N/10 NaOH required. (c.c.)	Lactic acid strength of sample.
5	1	20	0	18.70	71.90
5	2	20	0	21.70	83.44
5	3	20	0	22.55	86.71
5	4	20	40	23.15	89.01
5	5	20	40	23.20	89.21
6	1	20	0	18.65	71.75
6	2	20	0	21.60	83.09
6	3	20	0	22.60	86.94
6	4	20	40	23.20	89.25
6	5	20	40	23.25	89.44
7	1	20	0	18.70	72.71
7	2	20	0	21.50	83.59
7	3	20	0	22.25	86.51
7	4	20	40	23.10	89.82
7	5	20	40	23.10	89.82
8	1	20	0	18.35	71.25
8	2	20	0	22.45	87.17
8	3	20	0	23.75	92.22
8	4	20	40	24.30	94.35
8	3	20	40	24.35	94.55

TABLE II.

Showing the Results Obtained on Titrating Lactic Acid with Normal Alkali by Various Procedures.

No. of experiment	No. of procedure[4]	Amount of sample taken. (Gm.)	N/1 NaOH added before titration.[5] (c.c.)	N/1 NaOH required. (c.c.)	Lactic acid strength of sample. (Per cent.)
1	1	2.4280	0	19.50	72.28
2	2	2.4280	0	23.20	85.99
3	3	2.4280	0	23.35	86.55
4	4	2.4143	50	23.50	87.60
5	5	2.3649	50	23.12	87.99
6	6	2.3899	50	23.27	87.63

[4] Procedure No. 6 differed from No. 4 only in that the alkaline mixture was allowed to stand fifteen minutes instead of thirty, before titrating the excess alkali.

[5] Where no alkali was added before the titration an equal volume of water was added instead.

It appears from the results given in the above Tables that the titration of lactic acid at a boiling temperature is not only avoidable, but may even yield varying and considerably lower results than by the residual titration process. Further, the residual titration process is applicable even to dilute (about tenth-normal) aqueous solutions of the lactic acid when the amount of alkali added is about twice the amount necessary to neutralize all the lactic acid, and that practicably as close results may be obtained even if the mixture is not boiled but simply allowed to stand at ordinary temperature for half an hour before titrating the excess alkali; all of the samples of lactic acid examined showing a greater acid strength even by the latter procedure than when titrating at a boiling temperature and taking the end-reaction as that point when the color of the indicator will not completely disappear even by continuing the boiling for ten minutes longer. These results also show that the residual titration process indicates an acidity which is quite in harmony with the U.S.P. specific gravity requirement; while the fact that the present U.S.P. acidity requirement of 75 per cent. is only comparatively little above that which most of the samples examined showed (about 72 per cent.) on direct titration at ordinary temperature (procedure No. 1) and considerably below that shown by procedures Nos. 2 and 3 (about 83 to 86 per cent.), would indicate that the first appearance of neutrality was taken as the end-reaction by the author of the present U.S.P. method. It is also seen that none of the eight samples examined showed an acid strength of less than 87 per cent. when assayed by the residual titration process. A requirement of not less than 85 per cent. instead of the present requirement of not less than 75 per cent. would, therefore, come nearer the actual strength of the lactic acid on the market and would also fairly harmonize this requirement with the specific gravity requirement. Finally, it may be mentioned in this connection that, as shown by Utz,[6] lactic acid is volatile with water vapor and hence for this reason also it would seem best to avoid boiling its aqueous solution when it is desired to estimate its quantity. Likewise, from the point of view of the time required for the assay, the residual titration process is certainly not at a disadvantage in the comparison. For when titrating at a boiling temperature, from about twenty minutes (procedure No. 2) to about forty minutes (procedure No. 3) was

[6] *Chem. Zeit.*, **29**, 363–364 (1905).

required for each titration; whereas in the residual titration process not more than thirty minutes need be consumed for the corresponding part of the assay, and even during this time the attention of the operator is not required as closely and repeatedly for each titration as when the titration is carried out at a boiling temperature, and no attention at all is required from the operator during this period when the mixture is simply allowed to stand at ordinary temperature. It would seem, therefore, that the residual titration process has many advantages over the method in which the titration is carried out at a boiling temperature, which should justify its adoption in the next revision of the U.S.P. And since practically as close results are obtained by simply mixing well the acid with about twice the amount of alkali required and allowing the mixture to stand from fifteen to thirty minutes before titrating the excess alkali, as when the alkaline mixture is boiled for fifteen minutes, it would seem that the boiling might be entirely omitted, and the assay method for lactic acid modified to read somewhat as follows:

To about two grammes of the sample of lactic acid, accurately weighed, add 50 c.c. of normal NaOH, mix well, and let stand for half an hour. Then titrate the excess alkali by means of normal sulphuric acid, using phenolphthalein as indicator. The number of cubic centimetres of the alkali found to be required, multiplied by the lactic acid equivalent of 1 c.c. (0.09 Gm.), and this product divided by one-hundredth of the weight of the sample taken for the assay, will express in percentage the lactic acid strength of the sample.

A NOTE ON THE USE OF SULPHUR DIOXIDE IN CHECKING THE EQUIVALENCIES OF THE VOLUMETRIC SOLUTIONS OF IODINE, ALKALI, AND SILVER.

By Elias Elvove.

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In connection with some tests which are being carried out at the Hygienic Laboratory on the efficiency of a sulphur burning stove, designed by Dr. Norman Roberts and Mr. F. A. McDermott of this laboratory, the writer has had occasion to estimate the relative amounts of SO_2 and SO_3 formed in these combustions, by

the method of Kastle and McHargue.[1] This method depends on the reaction expressed by the equation

$$I_2 + SO_2 + 2H_2O = 2HI + H_2SO_4;$$

from which it is seen that for every equivalent of iodine two equivalents of acid result. Hence by determining both the amount of iodine used up in the reaction and also the total acidity after the reaction, we can estimate both the SO_2 and SO_3, since the found excess acidity over that required by the above equation would be a measure of the SO_3 originally present. In the work of Kastle and McHargue, the exact strength of the thiosulphate solution was determined by means of Kahlbaum's resublimed iodine immediately before each experiment and the exact strength of the iodine solution determined by means of the thiosulphate. The exact strength of the sodium hydroxide was frequently determined by means of weighed amounts of pure oxalic acid.

In this connection, it occurred to the writer that the above reaction between SO_2 and iodine might be used with advantage in checking the equivalencies of the standard iodine and hydroxide solutions; and if instead of using an approximate amount of potassium iodide ("about 18 Gm."[2] per litre) in the preparation of the iodine solution, an accurately weighed amount of KI (say 16.602 Gm.[3] per litre) were used, the purity of which has been accurately ascertained by means of the standard silver solution, the values of the iodine and hydroxide solutions could be directly compared, in the same solution, with the standard silver solution; which, as pointed out by the writer,[4] might be used with advantage in the standardization of all of the volumetric solutions ordinarily employed. And, since the value of the permanganate solution can be ascertained by titrating with thiosulphate (the strength of which is measured by the iodine solution) the amount of iodine which a definite amount of the $KMnO_4$ can liberate from a solution of KI acidified with sulphuric acid, if we prove the accuracy of our iodine solution in terms of the silver solution we can thus also check the accuracy of the value assigned to the permanganate solution. In

[1] *Amer. Chem. Jour.*, **38**, 465–475 (1907); and *Chem. News*, **96**, 236–238 (1907).

[2] Sutton: Volumetric Analysis, 9th ed., p. 133.

[3] This amount of KI per litre would yield a solution exactly tenth-normal (using the 1910 international atomic weights).

[4] *Amer. Jour. Pharm.*, **82**, 203–211 (1910).

other words the reaction between sulphur dioxide and iodine might be made, so to speak, the connecting link whereby the typical representatives of the four different classes of volumetric solutions, namely, the permanganate, iodine, alkali, and silver solutions, are connected together and their relative values established and referred back to the silver solution which was used in their first standardization.

The standardization and checking of the volumetric solutions as thus outlined seems especially advantageous in the case referred to above (the volumetric estimation of SO_2 and SO_3 when occurring together), for not only would we be able to refer all the results to one standard instead of two different standards (*e.g.*, iodine and oxalic acid), but we could also base the entire work on a standard which is more readily kept unaltered and is more convenient than is the case with solid iodine. Thus, for example, in the estimation of the SO_2 and SO_3 by the method of Kastle and McHargue, we might base the entire work on the value of our standard sulphuric acid solution. By means of the latter, the value of the NaOH solution could be readily ascertained; and by just decolorizing a definite amount of the iodine solution with a dilute, freshly prepared solution of sulphur dioxide (the strength of which need not be known) and determining the total acidity by means of the NaOH solution, we would obtain a check on the correctness of the assigned relative values of the iodine and hydroxide solutions; and since the resulting iodide could now be determined by means of the standard silver solution, we would thus obtain a check on the value of the iodine solution by direct reference to the standard silver solution. In this way we would not only avoid the weighing and handling of the solid iodine every time we want to check our solutions, but would also base the entire work on a *single* standard; and having found that when working with the solution of pure sulphur dioxide the results obtained are in close agreement with the theory, we could feel more certain when working in this way than when employing the double standard, that the subsequent results with the mixture of SO_2 and SO_3, however slight the variation may be from the results as obtained with the pure SO_2, are not due to any error in the standardization of our solutions, but solely to the presence of a small amount of SO_3.

The following data will illustrate the plan for standardizing all the ordinary volumetric solutions by means of pure metallic silver

as the ultimate standard and the subsequent checking of the equivalencies thus found, by means of the reaction between sulphur dioxide and iodine. All the solutions were prepared in the ordinary way except the iodine solution, in the case of which an accurately weighed amount of pure KI, 16.602 Gm. per litre, was used instead of "about 18 Gm." which is ordinarily used. Of this KI, 0.5442 Gm. was found equivalent to 32.7 c.c. of the N/10 $AgNO_3$ solution. This would make the iodine solution 99.85 per cent. tenth-normal with reference to its KI content, which value was used in the subsequent calculations. The water used was free from oxygen and carbon dioxide. When a fairly rapid current of SO_2 is available, the time required for obtaining about 50 c.c. of the sulphur dioxide solution, of a strength suitable for the present purpose, need not exceed fifteen seconds; hence no special care was taken to entirely avoid contact of the liquid with the atmosphere, but the SO_2 solution thus obtained was quickly transferred to a burette and used immediately for decolorizing the iodine solution. The following results were obtained by working according to the plan above outlined.

1. Used 0.4287 Gm. of the pure metallic silver (equivalent to 39.74 c.c. N/10 $AgNO_3$) and found it to require 39.62 c.c. of the N/10 NH_4CNS. Therefore, the normality of the NH_4CNS solution, expressed in percentage of an exact N/10 solution, is 100.30.

2. Found that 50 c.c. of the N/10 $AgNO_3$ are equivalent to 49.9 c.c. of the above N/10 NH_4CNS. Therefore, the normality of the $AgNO_3$ solution, expressed as above, is 100.10.

3. Found that 45 c.c. of the N/10 HCl are equivalent to 45.25 c.c. of the above N/10 $AgNO_3$. Therefore, the normality of the HCl solution, expressed as above, is 100.65.

4. Found that 45 c.c. of the above N/10 HCl are equivalent to 45.05 c.c. of the N/10 NaOH. Therefore, the normality of the NaOH solution, expressed as above is 100.54.

5. Found that 45 c.c of the N/10 oxalic acid are equivalent to 44.7 c.c. of the above N/10 NaOH. Therefore, the normality of the oxalic solution, expressed as above, is 99.86.

6. Found that 45 c.c. of the above N/10 oxalic acid are equivalent to 45.15 c.c. of the N/10 $KMnO_4$. Therefore, the normality of the $KMnO_4$ solution, expressed as above, is 99.53.

7. Found that 45 c.c. of the above N/10 $KMnO_4$ are equivalent to 45.45 c.c. of the N/10 $Na_2S_2O_3$. Therefore, the normality of the thiosulphate solution, expressed as above, is 98.55.

8. Found that 50 c.c. of the above N/10 $Na_2S_2O_3$ are equivalent to 49.5 c.c. of the N/10 iodine. Therefore, the normality of the iodine solution, expressed as above, is 99.55.

Control.—Used 25 c.c. of the above N/10 iodine. This was just decolorized by means of a dilute, freshly prepared aqueous solution of SO_2. On titrating the total acidity with the above $N/_{10}NaOH$, it was found to require 49.7 c.c. The solution was then acidified with 5 c.c. of 10 per cent. nitric acid, 55 c.c. of the above N/10 $AgNO_3$ added, and the excess silver in the filtrate determined by means of the above N/10 NH_4CNS. In this way, it was found that the total iodide in the solution was equivalent to 49.85 c.c. of the above N/10 $AgNO_3$ (or 49.9 c.c. of an exact N/10 $AgNO_3$). Subtracting from this 24.96 c.c. (the calculated value, in terms of N/10 $AgNO_3$, of the added KI in the 25 c.c. of the iodine solution), it would make the 25 c.c. of iodine equivalent to 24.94 c.c. of an exact N/10 $AgNO_3$.

Expressed in percentage of an exact N/10 solution, we would have as the value of the iodine solution by the SO_2 control, 99.76.

Corresponding value as found through the use of the above-mentioned intermediary solutions, 99.55.

On the basis of the iodine solution being 99.76 per cent. tenth-normal, it should have required 49.88 c.c. of an exact N/10 NaOH. Now, since only 49.7 c.c. of the above N/10 NaOH was required, it would show that the latter is a little stronger than tenth-normal.

Expressed in percentage of an exact N/10 solution, we would have as the value of the NaOH solution by the SO_2 control, 100.36.

Corresponding value as found through the use of the above-mentioned intermediary solutions, 100.54.

These results may be considered as showing a fair agreement between the first standardization by the silver solution, through the use of the above-mentioned intermediary solutions, and the SO_2 control, especially when it is remembered that an error of one drop in any of the measurements or titrations would correspond to a difference of about 0.1 to 0.2 per cent. It would seem, therefore, that the reaction between sulphur dioxide and iodine might be used as a convenient check on the found equivalencies of the iodine and hydroxide solutions in terms of the substance chosen as the ultimate standard—pure metallic silver.

REPORT OF THE PROCEEDINGS OF THE TENTH INTERNATIONAL CONGRESS OF PHARMACY, BRUSSELS, SEPTEMBER 1–6, 1910.*

By Reid Hunt,

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The opening session was held in the Palais des Academies September 1. More than 600 delegates, about one-half of whom came from countries other than Belgium, were present. Sixteen foreign governments had formally accepted the invitation to participate in the congress, and 20 were represented by official delegates. Delegates were present from the following American Republics: Argentina, Chilé, Venezuela, Guatemala, San Salvador, Haiti, and the United States.

The work of the congress was outlined at the opening meeting, at which the governor of Brabant, representing the minister of the interior; the president and secretary of the congress; and several of the foreign delegates, made addresses. The speakers emphasized, as the two subjects of greatest international interest: (1) The further unification of the pharmacopœias, with special reference to the adoption of uniform methods of assay of important drugs; and (2) the control of the sale of specialties (proprietary medicines), from the stand-point of public health as well as that of the material interests of the pharmacists. The governor of Brabant, M. Beco, formerly of the ministerial department having control of public health, hygiene, and pharmacy, urged the congress to add to its programme the subject of public hygiene, stating that he did not believe that pharmacists are as well qualified to deal with the problems of this subject as is desirable, and pointing out the possibilities of pharmacists securing for themselves a more privileged position if they will extend their activities beyond the narrower commercial pursuits.

The service of the Belgian Government in connection with the conference of 1902, which resulted in the securing of a greater degree of uniformity in the formulas of heroic medicines in the various pharmacopœias, was the subject of much favorable comment on the part of several of the foreign delegates.

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* Public Health Reports, volume xxv, No. 40, 1910, pp. 1406–1408.

On the succeeding days the congress met in two sections—scientific and professional. At each of these certain general questions, announced in advance, were discussed. A considerable number of communications, dealing for the most part with subjects of general scientific importance and all of international interest, were also presented. As a result of these discussions a number of resolutions were drawn up and voted upon, first by the sections and secondly by the entire congress at its concluding session September 6.

The first of the resolutions, presented by the scientific section, related to the unification of the methods for the assay of crude drugs and of galenical preparations, and for the determination of physical constants. The great importance of this subject, from the stand-point not only of medicine but also from that of international commerce, was emphasized. The congress requested the Belgian government to call an international conference for the unifying of the methods of analysis of the heroic medicaments; it also expressed the hope that, in the matter of alkaloidal assays, the commission would adopt, as far as possible, gravimetric methods. These conclusions and resolutions were based largely upon a paper by Doctor Schamelhout, who treated the subject from the stand-point of a practical pharmacist.

The second resolution related to the international unification of the reagents used in pharmacopœial work. It was pointed out how such a unification would aid in securing uniform analytical results and in the interpretation of the different pharmacopœias.

The third set of resolutions, which were adopted after prolonged and thorough discussion, related to the control of antiseptics, with special reference to the securing of commercial honesty and the safeguarding of the public. The congress expressed the opinion that such preparations should not be placed upon the market until they have been officially examined, both chemically and bacteriologically, and have received the approval of the departments of public health; that their efficiency should be determined and the claims made by the manufacturers be examined; that the amount of their active ingredients and their bactericidal strength should be stated, and that the sale of those claiming to possess therapeutic properties and of those containing poisons the sale of which is legally restricted should be limited to pharmacists.

The fourth resolution related to the introduction into the curricula of schools of pharmacy of courses on the analysis of certain

physiological and pathological secretions, especially of that of the feces. It was pointed out in the discussion that such work properly comes within the province of the pharmacist as a chemist and that it makes another professional bond between him and the physician.

The fifth resolution related to the preparation of galenicals by pharmacists. The latter were urged to make these preparations themselves as far as possible.

In addition to the formal reports a number of important scientific communications were made, some of which led to the adoption of further resolutions. Thus, as the result of a communication by Möller, it was resolved to advocate the adoption as an international standard of colors the standard of Klinchsieck and Valette. A paper by Hercod led to the adoption of a resolution in favor of the appointment of an international commission to establish a method for the standardization of pharmacopœial preparations of pepsin and for establishing a standard strength for this product.

A resolution was also passed expressing the opinion that it is desirable for the committees on pharmacopœial revision to publish each year supplements calling attention to the real scientific advances made.

Among the notable contributions made in the scientific section the following may be mentioned: Perrot, on the preservation of important plant drugs by the destruction of the intracellular enzymes; Leger, on the constitution of the aloins; Bourquelot, on glucosides; Goris, on plants containing caffeine.

The first of the resolutions presented by the section on professional interests related to the control of the sale of specialties. The basis for the discussion of the subject, which was prolonged and animated, was the very comprehensive report prepared by Breugelmans, Daminet, and Staes in which was reviewed the legislation on the subject in the leading countries of the world. Although the difficulties and complications which have arisen from the great increase in the number of such preparations and the problem resulting from the competition of manufactures were recognized, the discussion was limited largely to the phases which more directly concern the commercial side of pharmacy and especially to the subject of price protection. It was recognized that this is a question which will have to be solved by each country, but certain general principles were proposed, and the congress expressed the opinion that the sale

of medical specialties should, in all countries, be reserved to the pharmacists.

The second resolution presented by the section on professional interests related to the formation of an international pharmaceutical federation having for its purpose the protection of pharmacy as a profession and as an applied science. It was decided to appoint a commission to prepare a constitution for such a federation and to accept an invitation from the government of Holland to make The Hague its headquarters.

The third resolution related to the representation on pharmacopœial commissions of practical pharmacy, and the fourth to the limitation of the number of pharmacies.

It was also resolved to make the question of patents and trademarks one of the subjects for discussion at the next international congress of pharmacy.

In addition to the scientific programme, visits were made to the exposition, where the chemical and pharmaceutical exhibits of different countries were explained, and to dairies devoted to the production of milk for infants.

The members of the congress were the recipients of the most generous hospitality on the part of the officers of the congress and the pharmacists of Belgium.

THE PHARMACOPŒIA OF RUSSIA.

By M. I. Wilbert, Washington, D. C.

The new, sixth edition, of the Russian Pharmacopœia, published in 1910, is undoubtedly one of the more interesting books of its kind and it is perhaps unfortunate indeed that its appearance only in the Russian language makes it comparatively inaccessible to much the greater number of American Pharmacists. Fortunately, however, the official titles are Latin and the numerals in the formulæ are Arabic.

The general appearance of the book is all that could be desired; it is neatly bound and excellently well printed on a good quality of paper, and would generally be accepted as a thoroughly modern, up-to-date publication.

The book contains a total of XVIII and 591 pages with descrip-

tions of 617 official articles. The official articles include 162 botanical drugs, 15 drugs of animal origin, 195 chemical substances, 218 pharmaceutical preparations and 27 general descriptions.

The general descriptions are unique in that they include not alone general descriptions of types of pharmaceutical preparations but also descriptions of parts of plants, such as seeds, flowers, leaves and roots.

The Latin nomenclature has much in common with that found in the German Pharmacopœia, the new French Codex and the new Swiss Pharmacopœia so that there is even here a promise that the future will bring with it a proximation to international uniformity so far as the Latin names of widely used substances are concerned, even if it is, perhaps, Utopian to expect that we may yet have absolute uniformity.

Another indication that bodes well for the closer approximation of the several national pharmacopœias is the fact that this edition of the Russian Pharmacopœia like the ninth edition of the Swedish Pharmacopœia and the new third edition of the Italian Pharmacopœia was prepared in advance of the usual time of revision for the sole purpose of including the provisions of the Brussels' Conference Protocol.

The agreement adopted at the Brussels Conference for the unification of pharmacopœial formulæ for potent medicaments is reprinted entire in the prefatory pages to the book, and the provisions appear to have been generally adopted in all of the formulas included in the body of the pharmacopœia itself.

Among the titles representing the newer additions to our materia medica we find: Æthylum bromatum, Agar-Agar, Ammonium sulfoichthyolicum, Ammonium sozojodolicum, Antipyrinum, Chinosolum, Diuretinum (Theobrominum-natrio-salicylicum), Heroinum, Heroinum hydrochloricum, Phenacetinum, Salipyrinum, Salolum, Serum antidiphthericum, Sulfonalum, and Vaselinum.

Many of these titles illustrate the difficulties that we will be obliged to contend with for many years to come in developing names that are universally acceptable or applicable, because of the widely varying practices in connection with trade names and the protection given to individuals, in different countries, by laws governing trade-marks.

Chemical tests and assay processes have been given considerable attention and 33 pages are devoted to an enumeration of the reagents, volumetric solutions, and chemical apparatus necessary to apply the several official tests.

An appendix contains a number of tables including a list of potent medicaments, table of maximum single and daily doses, table of specific gravity of official liquids, and an alcohol table giving the per cent. of alcohol by weight and by volume of mixtures of alcohol and water at 15° C.

A double column index covering 32 pages completes a book that promises to be more than a passing factor in developing pharmacy in the country of its origin and will no doubt contribute much toward developing international unification of standards for potent or widely used medicaments.

BOOK REVIEWS

Abstract of Proceedings, United States Pharmacopœial Convention, 1910. Compiled and edited by the Secretary of the Convention. Published by the Board of Trustees, November 30, 1910.

Pharmacists and others who are interested in the Pharmacopœia of the United States will welcome this somewhat belated authoritative report of the United States Pharmacopœial Convention, primarily because of the information it contains, but also because it provides, for ready reference, a comprehensive and authentic account of the strenuous sessions of the Convention held in the City of Washington, in May, 1910, to provide for the revision of the Pharmacopœia of the United States now in force.

This abstract of the proceedings constitutes an octavo pamphlet of 110 pages, and in addition to a rather complete account of the actual happenings, presents verbatim reproductions of the several addresses and the reports of officers of the convention. In addition to the proceedings the pamphlet also contains:

1. A financial statement covering all of the receipts and expenditures during the period, from May, 1900, to May, 1910.

2. The Constitution and By-laws as revised by the Convention of 1910.

3. The official list of members of the U. S. Pharmacopœial Convention of 1910.

This latter list is particularly interesting in view of the unquestioned ruling of the Chair: "That anyone elected a delegate here, who has not come, is not a member of this Convention, cannot be elected a member of any Committee, nor as an officer."

To all intents and purposes this ruling limits membership in the Convention and official participation in the conduct of its affairs during the decennium to accredited delegates actually in attendance at the Convention.

Because of the information that it contains, this pamphlet should be widely distributed and should be frequently consulted by all who are interested in the Pharmacopœia of the United States and the development of its objects and its uses. M.I.W.

HYGIENIC LABORATORY BULLETIN NO. 70. A Study of Melting-point Determinations, with special reference to the melting-point requirements of the Pharmacopœia. By George A. Menge, Washington, Government Printing Office, 1910, p. 101.

This Bulletin is essentially a report on progress of a study of melting-point determinations made for and in co-operation with the Committee of Revision of the Pharmacopœia of the United States, and constitutes perhaps the most comprehensive review of this factor that has as yet been published, from a pharmaceutical point of view.

The various causes for divergence in the melting-point interpretations are reviewed and illustrated. The author also illustrates and figures the necessary appliances for a comparatively simple method that appears to be well adapted to present pharmacopœial needs.

The experimental data reported includes melting-point determinations on 24 official substances and amply suffices to show the need for adopting a definite and uniform method and procedure for determining the melting point of official substances if this factor is to be accepted as an indication of the identity or purity of official substances.

Pharmacists and chemists who are interested in pharmacopœial tests and requirements will find much in this Bulletin to assist them in determining the probable value of melting-point determinations in connection with official chemicals.

Copies of the Bulletin may be had on application to the Surgeon-General, U. S. Public Health and Marine-Hospital Service, Washington, D. C.

THE MICROSCOPICAL EXAMINATION OF FOODS AND DRUGS. A practical introduction to the methods adopted in the microscopical examination of foods and drugs, in the entire, crushed and powdered states. By Henry George Greenish, F.I.C., F.L.S., Professor of Pharmaceutics to the Pharmaceutical Society of Great Britain and Director of the Pharmacy Research Laboratory. With 229 illustrations. Second edition. Philadelphia: P. Blakiston's Son & Co., 1012 Walnut St., 1910. $3.00 net.

Professor Greenish is well known as an author of several standard works and a number of excellent papers. The present work is a laboratory manual, treating of the general technic employed in the microscopic examination of vegetable drugs and food products and giving a fairly large number of typical examples under each of the classes considered. There are some 15 sections, in which are considered: starches, hairs and textile fibres, spores and glands, ergot, woods, stems, leaves, flowers, barks, seeds, fruits, rhizomes, roots, adulterants of powdered foods and drugs and a general scheme for the examination of powders.

While the work is especially written for the students of the School of Pharmacy of the Pharmaceutical Society of Great Britain, it could be well adapted by teachers in other schools and colleges of pharmacy in their work. The following statement from the preface is deserving the attention of the teachers in those schools of pharmacy where the subject of pharmacognosy is not taught as a means to a practical end. "Before the microscopical examination of vegetable foods and drugs can be intelligently practised, a general knowledge of botany and a fairly sound and thorough acquaintance with botanical histology are absolutely necessary. It is as impossible for anyone to become a competent microscopist without such preliminary knowledge, as to become a competent analytical chemist without first acquiring a sound knowledge of the theory and principles of the science of chemistry. For this reason it appears to me that the training now given in the School of Pharmacy of the Pharmaceutical Society, comprising as it does, a knowledge of the principles upon which the sciences of botany and chemis-

try rest as well as training in the application of the knowledge thus acquired, is admirably adapted to fit a man to become an expert not only in the microscopical, but also in the chemical examination of foods and drugs." Again and again is one reminded in this work of Greenish's of the observation of Hassall in regard to the application of the microscope "that there is scarcely a vegetable article of consumption, not a liquid, which may not be distinguished by means of that instrument. Further, that all those adulterations of these articles which consist in the addition of other vegetable substances and which constitute by far the majority of the adulterations practised, may likewise be discovered and discriminated by the same process." Furthermore, Greenish calls attention to the fact that the "Investigations recently conducted by the Society at the request of the General Medical Council have also shown that the microscopical examination of powdered drugs yields results of far greater value in determining their identity and purity than such chemical data as the amount of ash yielded by them." In view of the splendid work done by Greenish this work will do much in making a rational consideration of the subject of pharmacognosy possible and cause students and pharmacists to be willing to devote a sufficient amount of time to the mastery of the principles involved in the work.

SUSAN HAYHURST.

The memorial exercises, held at the Philadelphia College of Pharmacy on November 15, 1910, in connection with the presentation to the college of a portrait of Dr. Susan Hayhurst, were a worthy tribute to this pioneer woman pharmacist, to whom the majority of the women graduates of the Philadelphia College of Pharmacy are indebted for the opportunity she gave them to acquire a knowledge of the practical side of pharmacy.

Dr. Hayhurst matriculated in the Philadelphia College of Pharmacy in 1879, at the age of 59, and graduated four years later. During her more than thirty years of service as apothecary of the Woman's Hospital of Philadelphia she gave employment to some sixty-five young women, a number of whom were present on this occasion and contributed to the testimonial held in honor of prob-

ably the first woman graduate to practise pharmacy in America if not the world.[1]

Shortly after the death of Dr. Hayhurst on August 7, 1909, some of the women graduates of the college, under the leadership of Miss Sarah L. Naly, her successor as apothecary of the Woman's Hospital, determined to have a portrait done in oil for presentation to the College. Early in November, 1909, they obtained the consent of the Board of Trustees to hang the proposed painting in the Museum of the College and soon thereafter the Committee of the women graduates secured the services of a Philadelphia artist, Miss Florence J. Newton, to execute the work. The portrait was made after a photograph of Dr. Hayhurst, taken but a few months before her decease by the well-known photographer, Mr. F. Gutekunst, assisted by the artist's personal recollection of her subject. A reproduction of the photograph is given in the frontispiece. The painting is a most excellent one, being about two-thirds life-size, and hangs in a prominent place in the Museum, selected by the women graduates.

The president of the College, Mr. Howard B. French, presided at the presentation exercises, and in opening the meeting referred to the splendid services of Dr. Hayhurst for the advancement of the Woman's Hospital of Philadelphia, and spoke of his personal knowledge of her work for the benefit of women in pharmacy and her noble example to her students and apprentices.

Professor Remington was to have presented the portrait on behalf of the women graduates, but was unavoidably absent and his address was read by Professor Kraemer. It was as follows:

Mr. Howard B. French,

President of the Philadelphia College of Pharmacy:

On behalf of the women graduates of the Philadelphia College of Pharmacy, we have much pleasure in presenting to the College this portrait of Susan Hayhurst, M.D., Ph.G., who was the first woman graduate of this College.

The long and useful career of our deceased friend was marked

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[1] Elizabeth Marshall, though not a graduate in pharmacy, was probably the first woman to practise pharmacy in this country (see this Journal, 1904, p. 271), and it is recorded that Dr. Mary Putnam Jacobi graduated from the New York College of Pharmacy in 1883, the year of Dr. Hayhurst's graduation, but it is probable that she never engaged in the practice, having become distinguished as a teacher and practitioner in medicine.—Editor.

by many acts of kindness and she made the path easy for many a struggling woman, striving for the coveted diploma of her Alma Mater. Dr. Hayhurst graduated from the Woman's Medical College in 1857 and from our College in 1883.

In her position as apothecary of the Woman's Hospital, she had the opportunity of giving practical instruction to girls who had chosen pharmacy for a vocation and her labors were more than appreciated, because for many years the dispensary of the Woman's Hospital was the only place where girls could secure practical knowledge of the business, owing to the prejudice which existed some years ago against women pharmacists.

As a student, Dr. Hayhurst was diligent in her efforts to acquire pharmaceutical knowledge. Until within the last few years of her life, she could be found poring over books and freely giving to her associates and younger women the information which she had obtained. She became a veritable mine of practical points.

Her disposition was kindly, yet when occasion required, she could express herself forcibly, particularly when some of the women would neglect some duty or commit, as she would say herself, "a pharmaceutical crime."

It is rarely given to any one to spend thirty odd years in teaching pharmacy but Dr. Hayhurst has this distinction, and it will be many years before her record of earnest, helpful, devoted service will be equalled. She was loyal to her Alma Mater to the last and she never tired of singing the praises of her beloved College.

To the women and girls who have had the benefit of her instruction the example of her beautiful life of service must be an inspiration. Gentle but firm, steadfast and unyielding in her devotion, she has gone on before, and Mr. President we now offer to you as the representative of this College, this portrait, believing that you will cherish it and give it a place among the portraits of those honored ones, who have testified their allegiance to the oldest and best College of Pharmacy in America.

In accepting the portrait, Mr. French said that it gave him great pleasure as president of the College to receive the portrait of Dr. Hayhurst and that it would find a place among the portraits of other leaders in American pharmacy on the walls of the College. He expressed his appreciation of the loyalty of the women graduates to their Alma Mater, and then called for the reading of a biographi-

cal sketch of Dr. Hayhurst by Miss Susannah G. Haydock, which will be published in the *Alumni Report* of the College. Additional remarks were made by Miss Naly, Dr. Anna E. Broomall, Mr. Charles C. Parsons, Mr. E. M. Boring, Prof. C. B. Lowe and Professor Kraemer.

The following sketch of Dr. Hayhurst is prepared in large part from the data secured through Miss Florence Yaple from various of her friends and relatives, especially her nephew, Mr. Walter F. Hayhurst, a lawyer residing in Lambertville, N. J., and extracts adapted from a sketch by Miss Sue P. Chambers which appeared in *Woman's Progress* some years ago (January, 1895).

Dr. Susan Hayhurst was a descendant of Cuthbert Hayhurst, a member and minister of Settle Monthly Meeting of Friends, in Yorkshire, England, who came to this country in the ship "Welcome" with William Penn; he died the year following and was buried September 2, 1683. His widow, Mary, took up certain lands which were allotted to him in Middletown Township, Bucks County, Pa., near the present village of Langhorne. Four generations later her father, Thomas Hayhurst, was born in this neighborhood, and married Martha Croasdale, also of an old Quaker family; he was a man self-educated, but of considerable ability and many talents. He was a surveyor and scrivener. He afterwards moved with his family to Wilmington and Camden, Delaware, where he engaged in the manufacture of "earthenware," and later engaged in the commission business in Philadelphia. He also engaged in school teaching, and about the year 1840 with his son, Jeremiah Hayhurst, the father of Walter F. Hayhurst, already mentioned, kept a select school at West Chester, Pa. There were eight children in the family and Susan was the second, having been born December 25, 1820, at Middletown, Pa.

Her schoolgirl days were passed at an institution in Wilmington, under the influence of "Friends." As a student she was particularly apt in mathematics and could recite verbatim any amount of text. She would have been considered an apt pupil, but when she came to teach found the want of that technical training which she afterwards obtained by taking the best instructor available in whatever study she wished to pursue.

She commenced teaching when quite a young girl, her first school being in Bucks County, Pa., near Newtown, and spent some years

in various country schools—an important and interesting portion of her life, as much of her time was spent with a class of people interested in the stirring events of that day, and many of them not lacking in intellectual culture. At one time she was a frequent companion of a skilled botanist, and together they became acquainted with the wild flowers of field and forest and meadow.

When her parents moved to Philadelphia, amongst her new acquaintances she found, in one of the professors of the Woman's Medical College, a very superior teacher of chemistry. To avail herself of Dr. Johnson's instruction, she entered the college for that and physiology, thinking to better qualify herself for teaching these branches. After some months' study, becoming deeply interested, she decided to take the entire medical course. To do this it was necessary to teach in the summer while attending lectures in the winter. Again she went to the country, where she found liberal-minded people and a devoted botanist. There she and her medical books were curiosities.

The last year of her course at college she was induced to take charge of the Friends' School at Fourth and Green Streets, Philadelphia, and was principal of that school when she graduated in medicine in 1857.

That graduation day would contrast greatly with one from the same college at this time. The medical woman of to-day knows little of the social ostracism that attended the pioneers in this profession. Now unnoticed in the crowd, or respected and even honored whenever they come to the front; in past days, even on the street, they were subject to indignities from their fellow students of other medical colleges. The commencement (numbering ten candidates) was a quiet affair, with a few friends who were brave enough to stand by those, who, better than they then knew, "were paving the way for liberal education." On this occasion, Prof. C. D. Cleveland, the writer on English Literature, then president of the college, came forward and stated that he had sought in vain in this city for a reverend who would take part in the services, and then himself—a layman—asked the Divine blessing on these young women who were about to enter an almost untried field.

Dr. Hayhurst still continued ten years at Fourth and Green Streets, then opened a school of her own with a class of fifty, many of whom had been her former pupils.

We next find her going West for a much-needed rest and change, and to visit friends. Then she was asked to organize a new public school in the town she was visiting, on the Philadelphia plan. Having finished this work and made the visit, she at the end of a year returned to Philadelphia, and with the intention of taking up the practice of medicine, entered the Woman's Hospital to familiarize herself with the advance ideas in medicine since her graduation.

She was solicited by the management of the hospital to take charge of its pharmaceutical department, a position of great responsibility, and entered on her new duties in 1876.

With her life-long habit of knowing—what may be known—of the subject in hand, and having turned away from that which she had intended as a life work, she again took up the student life in connection with daily service as pharmacist at the hospital. It was not her habit to leave anything undone in the way of investigation that could add to her efficiency, so she sought and obtained permission to matriculate at the Philadelphia College of Pharmacy.

No difficulty surrounded her attendance of these lectures. The boys were probably not glad to receive this one woman who entered a class heretofore occupied entirely by men, and who might mar their college freedom, but they made no offensive demonstration.

When she took her tickets it was a question whether the college would grant her its diploma, but on the completion of its course, she was graduated in 1883.

Professor Remington, in his valedictory address, said: "It is the best and largest class we have ever graduated, and we do what has never been done in the history of these sixty-two commencements, confer the degree on a woman." Then arose such a storm of applause as would have satisfied the most ambitious debutante. The large hall was filled in every part, and the graduates, 150 in number, seemed to vie with the audience in expressing their gratification.

The contrast in twenty-six years between these two commencements in which Dr. Hayhurst participated marks the advance of public sentiment. At the first when it was an innovation for women to enter the medical world, there were but ten graduates, a small audience, and no enthusiasm. A wide acquaintance with medical students made her influence far-reaching. From India, China and Japan came messages, gifts of rare and beautiful things, thanks

for advice given, for supplies of all kinds selected. Many a missionary owed the successful equipment for her work to this kindly care, either before she went or in answer to requests after she arrived in the foreign country. The purchase and manufacture of supplies for her own department in the hospital passed under Dr. Hayhurst's supervision, "and a care" at times was extended to matters not connected with drugs. To have seen her with hammer and screw-driver in hand one might have wondered if she possessed any of the characteristics of that ancestor who had "a very good mechanical head," according to his neighbor and friend, the one time Governor of New Jersey. All this busy life, yet it did not prevent an every summer devotion to a flower garden which furnished many a bouquet for friend and invalid, nor the taking up of a new study, or the critical pursuit of an old one.

Her reading was very wide, and she read very much poetry and fiction for her personal pleasure, but seemed to read science and history with quite as much satisfaction. Her method of thought was logical and she was interested intensely in all the questions of the day. She believed in Woman Suffrage, although not taking much active part in the movement, and sometimes regarding with amusement the methods of some of its advocates. She was intensely interested in the abolition of slavery, and afterwards in the elevation of the colored people. She was a consistent member of the Society of Friends and a regular attendant at meeting, although seldom taking any active part in the business.

It is stated that she met William Loyd Garrison, Wendel Phillips, the Burleighs, Lucretia Mott, and many other prominent anti-slavery advocates. In later years she was particularly intimate with Anna Jeans, the Philadelphia philanthropist and was consulted by her in the distribution of her charities.

In enumerating Dr. Hayhurst's activities reference should also be made to the fact that she was taught surveying by her father and that she assisted him in this line of work. Latterly her whole interest was centred in the Woman's Hospital; in addition to the duties of her regular position, she was frequently consulted by the managers and took an active part in raising funds for many improvements. She was particularly cheerful in her manner and enjoyed a joke. An incident is cited that when they were celebrating the "Silver Anniversary" of her employment at the hospital

some newspaper man wanted her age and she refused to give it. Afterwards she said that the reason she refused was the fear that the people would think she was getting too old to take an active part in business.

Dr. Hayhurst possessed marked social qualities, and was a member of the following societies: The Century Club, of which she was a charter member; The New Century Guild (both women's clubs); The Browning Club of Philadelphia, in which, however, her membership cannot be confirmed by the present secretary; The American Academy of Political and Social Science; The Woman's Suffrage Society of Philadelphia, and The Pennsylvania Pharmaceutical Association.

She was a good disciplinarian, and during all the years of her charge of the dispensary of the Woman's Hospital it was characterized by cleanliness, neatness and orderliness in every part. Not only this, she provided ample equipment in the way of pharmaceutical apparatus and always sought to use the most approved methods in the making of preparations, the majority of which were made by her assistants. She also considered it a part of her duty to look into the qualities of new remedies, and it is to her credit that very few, if any, of the fraudulent or worthless preparations offered for sale ever found their way into the dispensary of the Woman's Hospital. She always spoke of her assistants as "my girls," and was ever mindful of their interests, both social and intellectual, frequently inviting them to accompany her to the meetings of the societies of which she was a member.

At a meeting of the Board of Managers of the Woman's Hospital, held September 10, the following resolutions were offered:

Resolved, That in the death of our valued Friend, Dr. Susan Hayhurst, the hospital has lost a faithful and devoted worker; therefore

Resolved, That the thirty-three years spent in our midst will long be remembered by us, and her influence be felt, especially in the department over which she presided; the aim of her life was to further the interests, and widen the influence of the hospital, and by her faithfulness to this duty, she showed her love for it. While we miss her presence, we know that "our loss is her everlasting gain." Therefore,

Resolved, That a copy of these resolutions be entered on the Minutes of the Board, and a copy sent to the family.

THE CITY OF WASHINGTON BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The regular stated meeting of the City of Washington Branch of the American Pharmaceutical Association was held at the Hotel Raleigh on the evening of November 11, 1910, with the members of the Association of Official Agricultural Chemists as guests.

The subject under discussion was The Pharmacopœial Convention of 1910 and the prospective Pharmacopœia of the United States.

Dr. H. W. Wiley, the President of the United States Pharmacopœial Convention, presented a communication in the course of which he outlined his opinions regarding the Pharmacopœia and the methods to be followed in revising it.

Prof. Joseph P. Remington, the Chairman of the Committee of Revision, expressed the opinion that the Convention was indeed fortunate in having Dr. Harvey W. Wiley as its president and presented a short communication in the course of which he commented on some of the more important points referred to by Dr. Wiley and outlined the nature and amount of work that had been accomplished during the summer months.

Commenting further on the scope of the Pharmacopœia he expressed the belief that the real sentiment of both physicians and pharmacists was neither in favor of a skeleton pharmacopœia nor of a padded pharmacopœia, but of what he was pleased to designate as a sane pharmacopœia.

He then called attention to a prospective communication by Prof. Rusby, for the Association of Official Agricultural Chemists, in which he points out the need for having a book of standards for all drugs that are widely used, so as to facilitate and simplify the work of the United States Custom House officials in connection with the importation of drugs.

Prof. Remington also pointed out that for many years the Pharmacopœia was a closed book to the medical profession because its members had been lead away from it by the detail man of the manufacturer and proprietary medicine maker. The resulting decay of therapeutics has brought about a state of confusion and a tendency to therapeutic nihilism that he considers to be most unfortunate.

He holds that physicians do not know a sufficient number of U.S.P. preparations and do not appreciate the fact that their fellow practitioners in different parts of the country, and in different cities,

use totally different medicines, for which the Pharmacopœia of the United States should furnish standards.

Prof. I. V. S. Stanislaus, of Philadelphia, asserted that the paper by Dr. Wiley had been to him a revelation and a treat true and rare. He had been particularly impressed by the reference to needless duplication of drugs having similar properties and willingly endorsed the proposition to delete useless duplications from the Pharmacopœia.

He pointed out that the content of previous pharmacopœias represented the selection and dictates of the few and not of the many and expressed the hope that in the forthcoming Pharmacopœia greater care be exercised regarding admissions and deletions.

Dr. Murray Galt Motter, the Secretary of the Pharmacopœial Convention, discussed a number of the more important points embodied in the able, comprehensive and timely paper by Dr. Wiley and pointed out more particularly that the work and the function of the Executive Committee, as outlined by Dr. Wiley, was in accordance with the intent and purpose of the Board of Trustees of the former Convention.

He also pointed out that the professional representation on the General Committee of Revision was not alone interesting but rather significant. Of the total number 34 (indeed 35 when a vacancy was filled) were nominees of the pharmaceutical caucus and but 16 were nominees of the medical caucus. Of the latter it is also interesting to note that only 2 reached the executive committee.

In connection with the scope of the Pharmacopœia he pointed out that the Pharmacopœial Convention, by a vote of 95 to 47, emphatically recorded its conviction that substances "whose value and use have not been established" should not be included. And then, on the plea that it was unnecessary to hamper the Committee elected for the purpose of carefully selecting the list of substances, the Convention was induced to strike out, by a vote of 123 to 40, this "ambiguous and dangerous provision" thus leaving the final decision regarding scope with the members of the General Committee of Revision.

With reference to the business of the Pharmacopœial Convention he asserted that it had been pointed out by several observers that "the financial statement made to the Convention was in no wise satisfactory, explicit, or in justice to the intelligence of the body to which it was delivered." In commenting on "the enormous sales of the book amounting to nearly 40,000 copies the first year," he

pointed out that as a matter of fact the sales of the Pharmacopœia did not reach 40,000 until the middle of 1908.

In concluding he expressed the belief that if those who are to effect the work of revision do not clearly realize their responsibility to the Convention and to the several professions represented, and produce a book of standards indeed, but of standards for substances of established value and use, the next Pharmacopœia, instead of being a force, will be a farce.

Dr. Reid Hunt, Chairman of the American Medical Association Committee on the Pharmacopœia of the United States, pointed out that regarding the scope of the book there were two diametrically opposed views, both of which deserve consideration. The manufacturer and the pharmacist desire to have a book of standards that will include all of the substances that are, have been, or may be used as medicine, while the medical practitioner desires to have a book of standards for the approved therapeutic agents only so that the book may be used as a basis for instruction in medical schools and as a guide to the physician who is willing to adopt and use recognized standard remedies. It must be evident that these two objects are so totally different that it would be practically impossible to agree on a compromise and any attempt to do so would be considered a straddle that would be acceptable to but few.

He heartily endorsed the stand taken by Dr. Wiley regarding the scope of the book and expressed the belief that physicians and pharmacists should not be expected to furnish standards for Custom House officials and patent medicine manufacturers. As chairman of the Committee on the Pharmacopœia of the American Medical Association he had been able to get into communication with thousands of medical practitioners in various parts of the United States, all of whom were willing to use the best medicines that were available and desirous of obtaining authentic information regarding the probable efficiency of drugs.

Dr. Hunt outlined the methods that had been employed by his committee to secure the co-operation of the several sections of the American Medical Association, and referred more especially to the correspondence that had been had with medical men in active practice who were also teachers of materia medica and therapeutics in medical schools and colleges, and asserted that despite the fact that the evidence thus secured had been submitted through the Pharmacopœial Convention to the Committee of Revision, many of the members appeared to be willing to ignore the wishes of physicians and

the indications are that the scope of the forthcoming Pharmacopœia will again represent the views of but a limited number of individuals.

As an indication of the opinions held by the better informed medical men he quoted Dr. Abraham Jacobi, the Nestor of American physicians, who in discussing the content of the present Pharmacopœia deplored the fact that the makers of the Pharmacopœia were not willing to restrict the book to the best remedies only.

Dr. W. M. Barton seconded the remarks made by Dr. Hunt and asserted that he had also come to the conclusion that there are two diametrically opposed opinions regarding the scope of the Pharmacopœia and was satisfied that the book cannot, as it now stands, be accepted by medical men as a guide. He suggested the possibility of limiting the medical recognition of drugs by introducing a fair statement of the physiological action of the substance with each description.

Dr. Wiley, in closing the discussion, expressed himself satisfied with the feast of oratory that had been supplied to the members of the City of Washington Branch and their guests, and felt sure that nothing that he could add would tend to increase the appreciation of the importance of revising the Pharmacopœia of the United States along the lines laid down by the United States Pharmacopœial Convention.

M. I. Wilbert, Secretary.

REPORT OF THE CITY OF WASHINGTON BRANCH, COMMITTEE ON THE JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Your Committee, appointed to consider the paper by Mr. Joseph W. England entitled "*The Journal of the American Pharmaceutical Association*," greatly regrets to announce that, since its appointment at the October meeting of this Branch, the American Pharmaceutical Association has sustained a serious and irreparable loss in the death of Prof. C. S. N. Hallberg, the editor of the *Bulletin* and the chief Editor-elect of the proposed journal. This untimely death greatly complicates the problems involved in the launching of the new journal. While your committee was not specifically instructed to consider anything but the communication above referred to, it nevertheless feels that the occasion is an unusual one and that the late Editor's long years of disinterested service to pharmacy, and particularly the American Pharmaceutical Association, merit special recognition.

Your Committee would, therefore, respectfully recommend the adoption of the following preamble and resolutions:

WHEREAS, We, the members of the City of Washington Branch of the American Pharmaceutical Association, having learned of the death of C. S. N. Hallberg, a prominent member, and Editor of the Bulletin of our Association, are desirous of expressing our appreciation of his long continued and unselfish interest in everything pertaining to the advancement of the American Pharmaceutical Association and the progress of true pharmacy generally, now, therefore, be it

Resolved, That we hereby record our appreciation of his unfailing and untiring devotion to pharmacy, his singleness of purpose, and the unquestioned probity which guided his every effort in securing for true pharmacy the recognition properly due it.

Resolved, That a copy of these resolutions be embodied in our minutes and a copy forwarded to the family of the deceased as an expression of our sympathy and esteem.

The evidently authoritative communication, entitled "The Journal of the American Pharmaceutical Association," published in the October, 1910, number of the *Am. Ph. A. Bulletin* (p. 555), indicates that there are a number of important questions which appear, as yet, to have received insufficient consideration by the Committee therein referred to.

By far the most important of these several questions is the vacancy caused by the unexpected death of the newly elected Editor-in-chief. Professor C. S. N. Hallberg was generally conceded to be thoroughly well-fitted by his unusual training and experience to undertake the launching of this project, so fraught with possibilities for success or failure, for progress or retrogression, as the publication of a journal which will, inevitably, bring the Association into active competition with a number of drug and trade journals which have for decades been more or less influential in maintaining and developing the Association along the lines hitherto pursued.

That the position of Editor-in-chief and general manager of such a Journal is recognized as being the all-important factor, on which the success or failure of the enterprise must depend, is well indicated by the following opinion of a correspondent, himself well qualified by long years of experience to speak with authority:

"What the American Pharmaceutical Association needs is a man who has arrived, who understands every phase of journalism from the buying of paper and keeping tabs on the printer-man, all the way through soliciting "ads," preferred positions, writing top-heads and sub-heads, making up a page of reading matter in an artistic

manner, and so forth, all the way down to hiring and firing help and standing off the dissatisfied co-boss and the cantankerous advertiser or contributor. Such a man is rare and is *nascitur non fit,* and he has yet to go through a course of training to develop his technic at that."

The importance of this one question alone, the imperative need of securing for the prospective Journal an editor who is independent, efficient, fearless, and competent, would appear to your committee to be a sufficiently valid reason for deferring the publication of the new Journal from July 1, 1911, to January 1, 1912, so as to give the members of the Council of the Am.Ph.A. ample opportunity to canvass all of the several candidates, and to select from among them the one man most capable of meeting the requirements so tersely outlined above.

In addition to this self-evident reason for delaying the publication of the initial number of the proposed Journal, your committee would point out that there are a number of other reasons, any one of which should suffice to cause the Council of the Am.Ph.A. seriously to consider the advisability of deferring publication of the Journal until after the meeting of the American Pharmaceutical Association, in August, 1911. In order that this report may not exceed reasonable limits, but a few of these reasons may be mentioned and they but briefly:

For very practical reasons, it is advantageous to begin and end a volume of a periodical with the calendar year. The importance of this consideration is, perhaps, best appreciated by librarians and compilers, but even the casual reader must recognize the possibility of irritating mistakes and serious delays caused by incomplete references to articles in journals covering a portion of two calendar years.

The outline of the scope of the prospective Journal, as presented for the committee in the article referred to your committee, is altogether too general to be seriously considered by any association having the ideals and the aims of the American Pharmaceutical Association. The scope of the Journal, as thus outlined, would permit of a vacillating policy on the part of the editor or the committee on publication, both as to the reading matter and as to the kind and character of the advertising matter that is to be accepted.

In the opinion of your committee, the Council of the Association should also define the responsibility for material appearing in the reading pages of the Journal. We would suggest that it require

that all articles be signed, unless full and complete responsibility be assumed by the editor-in-chief. Such a policy would obviate possible misunderstandings and be a safeguard against anonymous communications.

Your committee would call attention to the proposed change in the size of the publication, as outlined in the paper under discussion. For upwards of fifty years the publications of the American Pharmaceutical Association have been in the widely used and convenient octavo form. The proposed change to quarto would necessitate rearrangement, and probably cause dissatisfaction in every library in which the publications of the Association are kept on file. Apart from the possible factor of economy, there is nothing whatever to recommend this proposed change.

Your committee would also beg leave to call attention to the fact that there appears to have been no provision made for publishing the report on the progress of pharmacy for the period between July 1, 1910, and June 30, 1911. We would recommend that this matter be published as a separate volume, in size uniform with the present bound volumes of the "Proceedings." We would recommend further that, for the period after July 1, 1911, this report be embodied in the Journal itself, so as to enhance the current value of the publication as much as possible.

Regarding the beginning of the publication on July 1, 1911, as heretofore decided upon, your committee would point out that the general scarcity of desirable original material in July would seriously militate against launching the Journal in the most presentable form at this time of the year, and would tend to hamper its influence by prejudicing both members of the Association and non-members at the very outset. On the other hand, we would point out that, in the event that the publication be deferred until after the annual meeting of the Association, the present Bulletin could be continued for all necessary announcements and news reports, and the initial numbers of the Journal be prepared in advance, so as to provide for the early publication of the original articles presented at the next annual meeting—even if it should be found necessary materially to enlarge the earliest numbers of the Journal, this would create a favorable impression.

To recapitulate, your committee heartily agrees with the sentiment that:

"In deciding to establish a Monthly Journal, the American Pharmaceutical Association has taken one of the most important

steps in its history, a step potential with large possibilities of good for American pharmacy."

It should be remembered, however, that in the event that this Journal should not prove to be all that its most ardent advocates expect it will be, but becomes an additional factor in hindering progress, instead of promoting the objects of the American Pharmaceutical Association, as paraphrased so tersely from the late Editor of the Bulletin, such a Journal might serve to stifle research, suppress knowledge, and discredit pharmaceutical education.

Your committee would, in conclusion, reiterate its original recommendation, that the Council of the American Pharmaceutical Association be importuned to defer publication of the Journal until opportunity shall have been afforded for the thorough discussion of these considerations.

In view of the urgent and far-reaching importance of this matter, your committee would recommend that the Secretary of the Branch be directed to forward copies of this report to the individual members of the Council of the American Pharmaceutical Association and to the pharmaceutical press.

Respectfully submitted,

(Signed) Lewis Flemer,
H. E. Kalusowski,
S. L. Hilton,
M. I. Wilbert.

Dec. 10, 1910.

The above report was unanimously adopted at the meeting of the City of Washington Branch of the American Pharmaceutical Association, held on the evening of Saturday, December 10, 1910.

In accordance with the instructions contained therein, I am sending you this copy. Respectfully,

M. I. Wilbert,
Secretary.

Washington, D. C., Dec. 17, 1910.

NEW ESSENTIAL OILS.*

Oil of Xanthoxylum alatum. From London we received under the name of "Chinese Wild Pepper" the fruit of *Xanthoxylum alatum* Roxb., a shrub belonging to the Rutaceæ, which occurs in the mountains of Northern Bengal as well as in China. Upon dis-

* From the Semi-Annual Report of Schimmel & Co. (Fritzsche Brothers), October, 1910.

tillation the fruit yielded 3.7 per cent. of a lemon-yellow oil with a peculiar odor, reminding of oil of water-fennel. Continued distillation yielded, in addition, 0.9 per cent. of a crystalline substance. We were compelled to abandon the attempt to dissolve this substance in the oil in the proportion indicated, because the bulk of the solid constituents again separated out even at a temperature of 25 to 30°. The properties of the oil and of the solid substance were therefore determined separately. The oil behaved as follows: $d_{15°}$ 0.8653, α_D — 23° 35′, $n_{D\ 20°}$ 1.48131, acid no. 9.9, ester no. 10.3, ester no. after acetyl. 33.6, soluble in 2.6 vol. and more of 90 per cent. alcohol. According to these analytical values the oil appears to consist chiefly of hydrocarbons, the nature of which remains to be elucidated by further investigation. The odor suggests the presence of phellandrene.

The solid substance which was obtained in the process of distillation, after being twice recrystallized from alcohol, presented colorless, odorless, optically inactive needles or leaflets, m. p. 83°. It was readily soluble in ether, chloroform, and acetone, a little less readily in alcohol, benzene, and light petroleum (all three of which solvents are very suitable for recrystallizing the body), and was insoluble in water. The substance is not an acid; it appears rather to be a phenol or lactone-like compound, as is evident from the fact that it does not react with solutions of alkaline carbonates, while it does react with those of caustic alkalies, from which latter it is again separated out by acidulation. Although when heated with benzoyl chloride it reacted violently, the yield of the resulting benzoyl compound was only slight, the greater part of the compound having remained intact. After repeated recrystallization from alcohol the benzoyl compound formed stout crystals, melting at 89°.

Dr. A. J. Ultée, of Salatiga, Java, has recently sent us a sample of an essential oil which we desire to describe here only briefly, as a detailed publication concerning its composition has been promised by Dr. Ultée himself.

Oil of Alpinia Galanga Willd. (Fam. Zingiberaceæ). This oil was of a lemon-yellow color and possessed a peculiar, strongly aromatic odor. Its constants were as follows: $d_{15°}$ 0.9847, α_D + 4° 20′, $n_{D\ 20°}$ 1.51638, acid no. 1.8, ester no. 145.6, soluble in its own vol. of 80 per cent. alcohol, opalescence ensuing upon the addition of 3 vols. According to Dr. Ultée, the oil contains pinene, cineol, camphor, and methyl cinnamate. The ester number of the oil indicates the presence of 42 per cent. methyl cinnamate.

FRONT VIEW OF THE PHARMACEUTICAL INSTITUTE OF THE UNIVERSITY OF BERLIN, WITH BOTANICAL GARDEN, FACING KÖNIGIN-LUISE-STRASSE IN STEGLITZ-DAHLEM, NEAR BERLIN.

THE AMERICAN
JOURNAL OF PHARMACY

FEBRUARY, 1911

CHEMICAL EXAMINATION OF THE ROOT OF LASIOSIPHON MEISSNERIANUS.

By Harold Rogerson.

A Contribution from the Wellcome Chemical Research Laboratories, London.

The genus *Lasiosiphon* belongs to the natural order of *Thymelœaceœ,* which, although containing about 300 species, appears to afford but one drug that has received the official recognition of any of the national pharmacopœias, this being the mezereon bark, from *Daphne Mezereum,* Linné, and other European species of *Daphne.*

The plants of the above-mentioned natural order are mostly shrubs, a few of which are found in temperate regions of the Northern Hemisphere, but which are more common within the tropics, and occur most abundantly in South Africa and Australia. They are remarkable, among other characters, for the great tenacity of the inner bark, and, in many species, the latter possesses extremely acrid properties.

In a " Revised List of the Flora of Natal," compiled by J. Medley Wood, and published in the *Transactions of the South African Philosophical Society,* 1908, vol. xviii, Part 2, p. 218, twenty species of *Lasiosiphon* are enumerated, of which, however, several are unnamed, and only their approximation to other recognized species is indicated. In the list referred to, the following is recorded respecting the plant under present consideration:

" *L. Meisnerianus,* Endl., Var. Inanda, 1800 feet alt., *Wood,* 36; Van Reenen, 5–6000 feet alt., *Wood,* 4520; var, near Durban, *Wood,*

1028; var., *Gerrard* and *McKen,* 807; near Durban, *Wood,* 104, 529; without precise locality, Krauss, 237. Compare also De Candolle's *Prodromus,* vol. xiv, p. 594, where the specific name of the plant is evidently more correctly written *Meissnerianus.*

In a work by Andrew Smith, entitled "A Contribution to South African Materia Medica," third edition, 1905, there are several references (pp. 35, 77, 125) to the plant designated by him as *Lasiosiphon Meisneri*—Kaffir, *isi-Dikili,* from which the following items of information respecting its characters and uses may be noted.

"The Lasiosiphons form a rather notable group. They have a heath-like appearance, with a tubular corolloid calyx, limb 5-parted. The flowers form a head with an involucre. The roots are very stringy and are used as sinnet. They are very scorching, if chewed, and will burn the tonsils and throat for twenty-four hours. Three species are used medicinally—*L. Meisneri; L. anthylloides;* and *L. linifolius.* The first of these is distinguished by its saffron or dark-orange flowers. Its leaves are three-quarters of an inch long, and less than one-eighth inch wide, hairy at the back. The involucral leaves are one-half inch long.

"*Lasiosiphon Meisneri* is a considerable bush. It is found in the lower basin of the Kat River, near its entrance into the Fish River, and is also found in various parts of Tembuland, being there used as a cure for snake-bite. The dose is from one-half to three-quarters of an ounce of the dried root, but some employ both leaves and root. The preparation is by infusion.

"It is somewhat difficult to say what its action in snake-bite precisely is, whether it is simply a powerful stimulant, almost blistering in its action, and long continued, and whether the same property does not explain the other uses of the plant. If a small fragment is chewed, it is nearly tasteless at first, but its burning quality is presently developed. Great caution must be used as to the quantity administered.

"*L. Meisneri* is also employed in cases of karroo fever, and a paste of the leaves for sores."

It has, furthermore, been noted by Smith (*loc. cit.,* p. 78) that "the root should always be used tolerably fresh, as it loses its virtue by long keeping."

One species of *Lasiosiphon,* namely, *L. eriocephalus,* Dcne., has been described in the "Pharmacographia Indica," vol. iii, p. 225. This is a native of the Deccan Peninsula and Ceylon, and is common

on the hills of Western India. The plant is a shrub, with leaves like the willow, and the bark is a powerful vesicant, this property being attributed to a resinous constituent.

The most recent notice of the *Lasiosiphons* appears to be that contained in a short paper on South African Plants which was contributed by Mr. G. E. Oliver to the *Chemist and Druggist,* London, April 25, 1908, p. 645. It is there stated that these plants are much esteemed among the natives for their tonic and blood-purifying properties, and also in the treatment of certain kinds of sore throat. The activity of the plant is said to reside chiefly in the root-bark, and with regard to the constituents of the latter Mr. Oliver has recorded the following observations: " A chemical examination of the root-bark shows it to contain a very small quantity of volatile oil, tannin (to which its virtue in sore throat would perhaps be attributable), and a resin, and it is apparently to this resin that its scorching properties are due, as it produces the sensation above referred to on the tongue, though it does not yield it to acidulated water when boiled with the latter. It contains no alkaloid."

EXPERIMENTAL.

The material used for this investigation consisted of the roots of the above-described plant, *Lasiosiphon Meissnerianus,* Endl., which had been kindly supplied by Mr. G. E. Oliver, of East London, Cape Colony, and was specially collected for the purpose.

The roots in question were more or less contorted and very irregular in size, some of the larger ones being as much as 10 centimetres (about 4 inches) in circumference. They were of a dark brown color, very rough and warty on the outer surface, and had a relatively thin bark, surrounding a lighter colored, very fibrous wood. As has previously been observed, when a little of the bark is chewed, a burning sensation is soon developed in the throat, which persists for several hours.

As a preliminary experiment, a small portion (10 grammes) of the ground material was tested for the presence of an alkaloid, but with a perfectly negative result.

Another portion (25 grammes) of the ground material was successively extracted in a Soxhlet apparatus with various solvents, when the following amounts of extracts, dried in a water-oven, were obtained:

Petroleum (b. p. 35–50°)	extracted.	0.20 Gm.	=	0.80 per cent.
Ether	"	0.45 "	=	1.80 " "
Chloroform	"	0.10 "	=	0.40 " "
Ethyl acetate	"	0.60 "	=	2.40 " "
Alcohol	"	2.10 "	=	8.40 " "
	Total,	3.45 Gm.	=	13.80 per cent.

For the purpose of a complete examination a quantity (29.94 kilogrammes) of the ground material was extracted by continuous percolation with hot alcohol, this operation having been kindly conducted by Messrs. Stafford Allen and Sons, of London. After the removal of the greater portion of the alcohol, a viscid, dark colored extract was obtained, amounting to 7.98 kilogrammes.

The whole of the above-mentioned extract was mixed with water, and distilled in a current of steam in a suitable apparatus for several hours, but no essential oil or other volatile product was obtained.

After the above operation there remained in the distillation apparatus a quantity of a dark brown resin and a dark colored aqueous liquid. The resin was separated by filtration, and well washed with hot water until nothing further appeared to be removed. The aqueous liquid and washings, on cooling, deposited a brown, resinous product, which was separately collected, and amounted to 320 grammes. A small portion (25 grammes) of this product was dissolved in alcohol, mixed with purified sawdust, and extracted in a Soxhlet apparatus with the following result:

Petroleum (b. p. 35–50°)	extracted,	*nil*		——
Ether	"	2.0 Gm.	=	8.0 per cent.
Chloroform	"	*nil*		——
Ethyl acetate	"	5.0 Gm.	=	20.0 per cent.
Alcohol	"	17.0 Gm.	=	68.0 per cent.
	Total,	24.0 Gm.	=	96.0 per cent.

These extracts were entirely resinous, and, although subjected to treatment both with acids and alkalis, nothing definite could be obtained from them.

The aqueous liquid, from which the resinous material had been completely removed, was concentrated to a small bulk, and shaken with ether, but only a trace of an amorphous product was thus ob-

tained. On subsequently shaking the liquid with amyl alcohol a quantity of amorphous material was removed. This was heated with a 10 per cent. solution of sodium hydroxide, the alkaline liquid being then acidified and extracted with ether, but it yielded nothing definite.

The aqueous liquid was then treated with a slight excess of a solution of basic lead acetate, when an abundant brown precipitate was produced. This was collected, well washed with water, then suspended in water, and decomposed with hydrogen sulphide. On filtering the mixture, and concentrating the filtrate, a resinous product was obtained which responded to the usual tests for tannic matter.

The filtrate from the basic lead acetate precipitate was treated with hydrogen sulphide for the removal of the lead, and the clear, filtered liquid evaporated to a small volume. It was found to contain a quantity of sugar, since it readily reduced Fehling's solution, and yielded *d*-phenylglucosazone, melting at 204–205°.

Examination of the Resin.

The resin which had been separated from the aqueous liquid, and thoroughly washed with hot water, as above described, amounted to 3685 grammes, thus corresponding to 12.3 per cent. of the weight of the drug. It was a brown, powdery substance, which, when inhaled, had an irritating effect on the nostrils, and when brought on the tongue, especially in alcoholic solution, a burning sensation was soon developed, similar to that produced on chewing the bark of the root.

For the examination of this resin a quantity (300 grammes) of it was dissolved in alcohol, mixed with purified sawdust, and the thoroughly dried mixture then successively extracted in a Soxhlet apparatus with light petroleum (b. p. 35–50°), ether, chloroform, ethyl acetate, and alcohol.

Petroleum Extract of the Resin.

This was a dark green, amorphous mass, amounting to 26 grammes. It was dissolved in alcohol, and heated for about four hours in a reflux apparatus with an alcoholic solution of potassium hydroxide. The alcohol was then removed, water added, and the alkaline mixture extracted with ether. The ethereal liquid was washed, dried, and evaporated, when a small amount of a crystalline

substance was obtained, which separated from alcohol in plates, and gave the color reaction of the phytosterols. On recrystallizing the substance from a mixture of ethyl acetate and dilute alcohol it was obtained in the form of flat needles, melting at 132–133°.

0.1188, when dried at 110°, lost 0.0056 H_2O. $H_2O = 4.7$
0.1132 of anhydrous substance gave 0.3468 CO_2 and 0.1250 H_2O.
$C = 83.5$; $H = 12.2$
$C_{27}H_{46}O,H_2O$ requires $H_2O = 4.5$ per cent.
$C_{27}H_{46}O$ requires $C = 83.9$; $H = 11.9$ per cent.

This substance is thus seen to be a phytosterol, and a determination of its optical rotatory power gave the following result:

0.2722 of anhydrous substance, made up to 25 c.c. with chloroform, gave $\alpha_D - 0° 40'$ in a 2 dcm. tube, whence $\alpha_D - 30.6°$.

The acetyl derivative, when crystallized from acetic anhydride, separated in needles melting at 110°.

The alkaline liquid from which the above-described phytosterol had been extracted by means of ether was acidified and again extracted with ether, the ethereal liquid being dried and the solvent removed. A quantity of fatty acids in the form of a dark green mass was thus obtained. These acids were distilled under diminished pressure, and, by means of their lead salts, were separated into solid and liquid portions. The amount of solid acid obtained was 3 grammes. It distilled between 220 and $230°/_{15mm.}$, and, when recrystallized from ethyl acetate, melted at 64°.

0.1320 gave 0.3634 CO_2 and 0.1470 H_2O. $C = 75.1$; $H = 12.4$
$C_{16}H_{32}O_2$ requires $C = 75.0$; $H = 12.5$ per cent.

The solid acid thus appeared to consist of nearly pure palmitic acid.

The liquid acids distilled between 215 and $225°/_{15mm.}$ and amounted to 2.5 grammes. Determinations of the iodine and neutralization values gave the following results:

0.2276 absorbed 0.2308 iodine. Iodine value = 101.4
0.2034 neutralized 0.4025 KOH. Neutralization value = 197.9
$C_{18}H_{34}O_2$ requires Iodine value = 90.0; Neutralization value = 198.9

These results indicated that the liquid acids consisted chiefly of oleic acid, with a very small amount of an acid of a higher degree of unsaturation.

Ether, Chloroform, Ethyl Acetate, and Alcohol Extracts of the Resin.

These extracts were dark brown, resinous masses, and amounted to 24.7, 35.0, 47.0, and 150 grammes respectively.

The ether and chloroform extracts were examined by shaking their respective solutions successively with aqueous sodium carbonate and sodium hydroxide. Furthermore, all the above-mentioned extracts were heated with 5 per cent. sulphuric acid in aqueous alcohol, and with a 10 per cent. solution of sodium hydroxide, but by none of these methods could any definite product be obtained from them.

Fusion of the Resin with Potassium Hydroxide.

A quantity (25 grammes) of the powdered resin was gradually introduced into 150 grammes of potassium hydroxide in a state of fusion, and the temperature of the mixture maintained at about 260° for some time. After cooling, the mass was dissolved in water, the solution acidified with sulphuric acid, and distilled in a current of steam. The distillate contained some volatile acid, which was converted into a barium salt, the latter amounting to 2.5 grammes. An examination of this salt showed the volatile acid to consist chiefly of a mixture of formic and butyric acids.

After the removal of the volatile acids, as above described, the liquid in the distillation flask was separated by filtration from a quantity of resinous material, and extracted with ether. The ethereal liquid was then shaken successively with a solution of sodium carbonate and a 10 per cent. solution of sodium hydroxide. The sodium carbonate liquid was acidified and extracted with ether, but on evaporating this ethereal liquid only a small amount of a tarry residue was obtained, the solution of which gave a green color with ferric chloride. The solution of sodium hydroxide removed nothing from the ethereal liquid, and on finally evaporating the latter a small amount of a dark colored, amorphous product was obtained, which possessed an exceedingly unpleasant odor.

Notwithstanding the very complete examination to which the roots of *Lasiosiphon Meissnerianus*, Endl., have been subjected, it will be seen that they have yielded but little of chemical interest. The chief constituent of the root is an amorphous resin, to which, as had previously been observed, its acrid properties are evidently due.

In conclusion, the author desires to express his indebtedness to Dr. F. B. Power for having suggested this research, and for the kind assistance he has afforded throughout the course of the work.

THE PREPARATION OF THYROID EXTRACT FOR THERAPEUTIC PURPOSES.

By S. P. Beebe, Ph.D., M.D.

During the last ten years there has been a marked increase in the interest shown toward the physiology of the internal secretions, and the therapeutic value of organ extracts has been the subject of much debate. The thyroid gland has been the centre of much of this discussion and its usefulness as a therapeutic agent in other conditions than those of the classical myxœdema has been demonstrated so thoroughly that the demand for a standard preparation may no longer be ignored. The manufacturers at the present time supply a variety of thyroid products prepared by different methods, and undoubtedly of differing therapeutic effects. The terminology shows great confusion and the precise nature of the substance that is provided is generally not known. For instance, the term iodothyrine which was used by Baumann [1] to describe the substance which he obtained by hydrolyzing thyroid glands with ten per cent. sulphuric acid. This substance was found to make up 2–5 per cent. of the glands by weight, it was insoluble in acids, soluble in alcohol and alkalies, contained 9.3 per cent. iodine, and from the experiments of Roos it was thought to represent all the physiological activity of the gland. The same term, "thyreoiodin," was used by Roos [2] to indicate "the alcoholic precipitate of a glycerin extract of the well-pulverized gland dried at body temperature." In Merck's index for 1907 iodothyrine is the name given to "milk sugar trituration of the active constituent of the thyroid gland, 15 grains of which contain 1/200 grains of iodine." In some instances supposed thyroid preparations have been found to consist of meat proteids impregnated with potassium iodide, or a poor quality of gland has been enriched by the addition of inorganic iodine.

The experience of clinicians confirms the belief that the commercial preparations are not uniform and that they are at times entirely inactive. Analyses of many preparations now on the market have

been made in this laboratory for the iodine content and it has been found that the products from various firms differ widely in the content of iodine, and also that the same preparations vary from time to time.

The precise relation which iodine has to the physiology of the thyroid has been a subject of much discussion and in a recent Bulletin from the Hygienic Laboratory Hunt and Seidell have reviewed the arguments pro and con in regard to this matter, and have given the results of a long series of experiments based upon a new method to show that there is a very close relation between iodine content and physiological activity. The precise function of the gland need not be called in question in discussing this point. We know that the thyroid gland has a very marked selective absorption for iodine. In this laboratory we have made many analyses to determine the iodine content of liver, kidney, and muscles taken from animals to which large quantities of potassium iodide had recently been given and have not found the slightest trace of it, while in the same animals the thyroid gland may have had its iodine content increased by 200–600 per cent. *In vitro* there is no more difficulty in iodizing a proteid from these other tissues than from the thyroid, so that Blum's [4] belief that proteids artificially iodized *in vitro* should be considered identical to those formed *in vivo* in the thyroid certainly has no justification.

(Blum has maintained the theory that the function of the thyroid is to detoxicate certain metabolic toxins by combining iodine with them, and in part bases the theory upon the experimental finding that thyroid extract which has been saturated with iodine *in vitro* no longer has the same physiological action that it does before the artificial saturation with iodine. From this finding he reasons that the addition of iodine destroys the toxic properties of the substances brought to the gland in the circulation, and that the more completely this is accomplished the less toxic the products are. The fallacy of this argument is to be found in the fact that iodizing of a proteid *in vitro* is a drastic chemical process in no way to be compared with the physiological action of the thyroid gland.)

No artificial product has ever been prepared which has the same effect upon metabolism, myxœdema, and cretinism that is obtained by iodized proteid from the thyroid gland. The discussion of the pharmacological action and therapeutic value of thyroid preparations need not involve us in discussion of the function of the gland.

DOES THYROID PROTEID FREE FROM IODINE HAVE ANY FUNCTIONAL ACTIVITY?

This is an old question and it has been the opinion of many experimenters from Baumann, Miwa, Stoeltzner, and Neumeister, and it has recently been reiterated by Jolin, that because many instances of iodine-free thyroids were found in animals enjoying apparent health, that therefore no essential relation exists between iodine content and physiologic action. Hunt [3] has modified this opinion somewhat by concluding that iodine-free thyroid has a mild degree of activity, but that it is not to be compared with normal iodized thyroid in its protective power to acetonitril poisoning.

Such a conclusion as well as that of the older investigators is, however, open to the criticism that the methods for determining the presence of iodine may have been faulty. A large number of thyroid glands have been analyzed for iodine in this laboratory during the last three years and we have not found any which were absolutely iodine free. There is no question that such a finding is due to an improvement in the Baumann method of iodine determination. According to the Baumann [5] method the thyroid tissue is fused in a nickel crucible with sodium hydroxide and sodium nitrate. Only sufficient sodium nitrate is used to give a clear fusion mass. The melt is dissolved in water, acidified with sulphuric acid, nitrous acid added to set free the iodine, which is shaken out with chloroform or carbon bisulphide and estimated colorimetrically. Dr. L. W. Riggs,[6] working in this laboratory, has shown that during the fusion process a variable amount of the iodine is oxidized to iodate, which is not subsequently reduced by the nitrous acid, and which, therefore, is lost in the extraction with carbon tetrachloride and gives too low a reading.

$$5\ NaI + NaIO_3 + 3H_2\ SO_4 \longrightarrow 3I_2 + 3Na_2\ So_4 + 3H_2O$$

According to the above reaction five molecules of iodide set free the iodine from one molecule of iodate, and it follows that where the proportion of iodate is greater than this some of it must remain undetermined. When small quantities of iodine are present in the fusion mass a relatively larger proportion of the iodine is oxidized to iodate and the proportion of one molecule of iodate to five of iodide is exceeded, with a consequence that iodine is lost. When only very small quantities of iodine are present it may be entirely oxidized, and a report given of no iodine found in the gland. The

improvement which Dr. Riggs has introduced is the addition of an active reduction by Devarda's alloy of the solution of the fusion mass, thus reducing the iodate to iodide and insuring a full yield. The figures given in his paper show that it is with the glands containing only a very small quantity of iodine that the largest errors are made. For instance, with sheep thyroids, which contained only .03 mg. iodine per gramme of fresh gland, 77 per cent. of the iodine was found after reduction. Subsequent experience has borne out these findings and we have repeatedly had glands for analysis which were found to be iodine free by the older method, but were found to contain marked quantities of iodine after reduction. In no instance have we found a thyroid gland free from iodine, and we have analyzed a wide variety of thyroid glands during the last two years. In view of these facts I am of the opinion that we are not at present justified in saying that iodine-free thyroid has an effect similar to that obtained by the normal iodized product, and, furthermore, it seems probable that many of the results ascribed to iodine-free thyroid are really caused by a proteid containing only an exceedingly small quantity of iodine. The recent paper of Hunt and Seidell [3] gives the most striking evidence yet published that iodine-free thyroid does have the characteristic metabolic effect of the iodized gland, but I believe the explanation of their results is to be found in the fact that their method of determining iodine was faulty, and the quantity of material used for iodine analysis too small.

These authors are agreed, however, that iodine-containing thyroid is much more effective than iodine-free thyroid, and give figures to show that the physiological effect is in direct proportion to the iodine content. Such a conclusion is in harmony with the findings of most students of this subject and agrees with the experiments made in my laboratory. I regard it, therefore, as probable that functional activity is proportional to iodine content, other factors being the same.

The thyroid gland contains a variety of protein substances which contain iodine and according to some investigators other iodine-free proteids. The methods of isolating these proteins have not been uniform and as a result it seems probable that authors have given different names to the same substances. The most conclusive work upon the chemistry of the thyroid has been done by Oswald,[7] who is led to conclude that thyreoglobulin is the characteristic iodine-containing proteid found in the gland. He describes another pro-

teid, which he names nucleoproteid, free from iodine and without functional activity. In my laboratory we have used various methods of fractioning the extracts from different types and species of thyroid gland in the hope of obtaining a series of proteids varying somewhat in composition and physiological activity. Such a series we have obtained, but, contrary to Oswald, in no case have we found nucleoproteid or other proteid free from iodine nor have we found any of the primary or secondary albumoses obtained on digestion to be free from iodine. When tryptic digestion, or acid hydrolysis is carried beyond the biuret stage a variety of fragments containing iodine are obtained. Even in extracts from perfectly fresh glands the filtrates obtained after removing the heat coagulable proteids contain iodized peptones, and if the glands are not fresh the amount of these peptone-like substances is much increased.

It is evident, then, that when the whole thyroid gland is ground, dried, and pulverized for therapeutic use that a variety of iodine-containing proteid and non-proteid substances is included. Are they all necessary or equally valuable physiologically, and may it not be that some of them are actually harmful? In an endeavor to answer these questions and also to determine the best method of preparing the physiologically active portions for therapeutic use we have made many experiments. I shall not describe in detail the many methods employed to fractionate the proteids, but will outline the procedure which we have finally hit upon as the simplest and most effective for preparing thyroid extract for therapeutic use. We have used glands from sheep, beef, and pig. In so far as we can judge by the gross appearance only normal glands are selected and this I think is a valuable point, as heretofore only sheep glands have been used therapeutically and it became evident very early in this work that sheep from certain regions always had goitrous glands poor in iodine. Moreover, it was these glands that the abattoir preferred to furnish since they were sold by the pound and the glands necessary for a pound were more easily obtained if goitres were used. I have seen such glands in the course of preparation into thyroid extract at two commercial laboratories. Such glands are rich in proteid of the thyreoglobulin type but very poor in iodine. Obviously here is an adequate source for much of the variation of thyroid preparations. The normal glands are obtained in as fresh a condition as possible and are kept from autolysis by freezing. They are ground to a fine pulp and extracted with three to four

times their volume of normal saline solution made very faintly alkaline by sodium hydroxide. Three or four drops of a ten per cent. solution of sodium hydroxide are added to every litre of salt solution. The extract is shaken vigorously at room temperature for one or two hours and is then transferred to the refrigerator, where it is allowed to remain for twelve to eighteen hours. At the end of this time a large portion of the proteid has been dissolved by the saline. The clear extract is obtained by filtering first through gauze to remove the larger fragments and then through paper pulp by the help of a Buchner funnel, after the method of Osborne. As stated before, this extract contains a variety of proteids and proteid fragments and our object is to separate the pure iodine containing globulin from the other constituents by as brief and simple a method as possible. This may be accomplished by salting out the proteid, filtering and finally dialyzing the precipitate, a procedure which requires a great deal of time and which exposes the product to abundant opportunities for infection and decomposition. The plan we have finally adopted is to acidify with acetic acid and heat to 44° C. for 10 minutes. Extracts of the different species of glands behave in characteristic fashion. The addition of acetic acid to extract of sheep glands gives a scanty precipitate or none at all; such as does form may be filtered out and is found to be richer in iodine than any fraction obtained subsequently. On heating an abundant flocculent precipitate is obtained at 44° C. This precipitate is rich in iodine, it dissolves readily in a weak alkaline solution, and is precipitated again by acetic acid. Its behavior with regard to dialysis and salt precipitation is that of a globulin; it contains more iodine than any proteid obtained from the filtrate heating to a higher temperature, and is by far the most abundant proteid in the gland. If this proteid is removed by filtration and the filtrate heated to a higher temperature, a further precipitate is obtained at 65°–70°, a third at 82°–86°, and a fourth after boiling for some time. All of these proteids contain iodine but in relatively much less amount than in the precipitate at 44°, they form only a small part of the entire proteid content, and they do not redissolve in a weak alkaline solution.

After all coagulable proteids are removed the filtrate contains substances giving the proteid color reactions and containing a by no means negligible quantity of iodine. If the whole gland extract is used for therapeutic purposes it follows that all of the various iodized fractions are administered. I believe that some of these sub-

stances not only give no *beneficial* therapeutic action but are actually harmful.

The following experimental evidence is offered in partial substantiation of this statement. Four lots of guinea pigs were given identical amounts of iodine, .0001 mgm. of iodine for each 100 grammes body-weight. The first lot in the form of purified thyreoglobulin, precipitated from the protein extract by acidifying with acetic acid and heating to 44° C. The second lot in the form of the alcohol-soluble portion of the filtrate from the pepsin digestion of the glands. The third lot in the form of the alcohol-soluble portion of the residue from the pepsin digestion of the gland. The fourth lot from the alcohol-soluble portion from extracts from normal glands after removing all the coagulable proteid. The second and fourth fractions give all the proteid color reaction, but compared with the nitrogen content they contain relatively much less iodine. The third fraction corresponds to iodothyrin, and as will be seen it is very rich in iodine. To be certain of the dose which each animal received, the administration was by hypodermatic injection in each instance. The relation of iodine to nitrogen in each of these substances was as follows:

1. *Sheep thyreoglobulin.*
   1 c.c. solution contains 1.25 mgm. nitrogen.
   1 c.c. contains 0.012 mgm. iodine.
   1 gramme nitrogen contains .0096 gramme iodine.
2. *Pepsin digestion filtrate, alcohol-soluble portion.*
   1 c.c. contains 7 mgm. nitrogen.
   1 c.c. contains .0375 mgm. iodine.
   1 gramme nitrogen contains .00535 gramme iodine.
3. *Pepsin digestion residue, alcohol-soluble portion.*
   1 c.c. contains 0.14 mgm. nitrogen.
   1 c.c. contains .09 mgm. nitrogen.
   1 gramme nitrogen contains .6428 iodine.
4. *Alcohol-soluble portion of extracts from sheep glands after removing all coagulable proteid.*
   1 c.c. contains 10.22 mgm. nitrogen.
   1 c.c. contains .044 mgm. iodine.
   1 gramme nitrogen contains .0043 gramme iodine.

The pigs receiving iodine in the form of the thyreoglobulin increased fifty per cent. in weight during the experimental period, which lasted nearly two months, and had no pathological disturbance

whatsoever from the injections. They were scarcely to be determined from the control pigs that received no injections whatsoever. The pigs receiving the alcohol-soluble portion of the filtrate from pepsin digestion lost weight, and all three died during the first month with a large loss of weight. The pigs receiving the alcohol-soluble portion of the pepsin digestion residue, corresponding to iodothyrine, increased in weight like the normal animals and were not to be distinguished from the animals receiving the proteid injections. Those animals receiving the alcohol-soluble portion of the extract from the sheep glands from which all coagulable proteid had been removed gained somewhat in weight, but one died in convulsions before the experimental period was over, while the other two were not to be compared with the control pigs. From these results we must conclude that the second and fourth fractions were toxic. Their precise nature we do not know, but the behavior is that of a simple peptone. Somewhat similar results have been obtained from other of the cleavage products, and further experiments have given us conclusive evidence that these substances are, in proportion to their iodine content, not to be compared with the thyreoglobulin in protecting mice from acetonitril poisoning. The extensive experiments of Cunningham [8] give facts which coincide with the results obtained in this laboratory: *viz.*, the autolyzed thyroid gland contains toxic substances.

Since the discovery of iodothyrine, it has been generally considered that this substance is the physiologically active principle of the thyroid gland, and that all the effects upon metabolism peculiar to thyroid activity could be duplicated by the administration of this substance by mouth. It is the writer's opinion that such a conclusion is not justified by the facts.

The physiologically active substance in the thyroid is elaborated by the active cells lining the alveoli, and it seems probable that under normal conditions a considerable amount of this substance is secreted into the alveoli and retained there as reserve material. It may, however, pass from the gland cell directly into the blood and in some pathological conditions we find practically no colloid, but an unusually well vascularized, actively proliferating parenchyma, associated with symptoms of over-activity of this gland. As we find the secretion in normal glands it is not in the form of iodothyrine, but in the form of an iodized proteid, and a drastic chemical process is required to liberate the iodothyrine. Furthermore, the secretion

enters the blood directly and not through the stomach. To imitate the physiological conditions I am convinced that we should administer the same biological sort of thyroid proteid by hypodermic injection. The human patient should receive human thyroid proteid by hypodermic injection. Of course such a conclusion is of theoretical interest only, but during the last three years I have had many opportunities to compare upon human subjects the effects produced by administration of various forms of thyroid preparations and from these observations the only possible conclusion is that the human thyroid is by far the best for the human subject. When we give the human thyroid extract we give a substance ready for instant use, and a comparatively small quantity will act more effectively from the qualitative and quantitative stand-point than a larger quantity of any other kind of thyroid material. These other forms probably act very largely by stimulating the gland of the individual to whom they are administered.

In its effects upon simple goitre, myxœdema, cretinism, athyroid symptoms found occasionally in the later periods of exophthalmic goitre, and various metabolic disorders associated with hypofunction of the thyroid, there is no other substance which acts so economically and efficiently as the proteid precipitated from extracts of normal human thyroid glands by acetic acid and heat to 44° C.

For the reasons above outlined we should use only the proteid obtained by a similar method from animal glands. Accordingly the original precipitate is washed repeatedly with normal saline by decantion or centrifugation until the wash-water is free from biuret reacting substances. It is then dissolved by the addition of a little sodium hydroxide, the solution filtered through a thick paper mat and again precipitated by acidifying with acetic acid. Heat is rarely required for the second precipitation. The washing process is repeated and more proteid-like material removed from the precipitated globulin. The final washed precipitate is centrifugated or filtered out and dried at low temperature, or it may be kept in solution and after filtration through a Berkefeld kept for hypodermic administration.

Proteids have been prepared in this manner from glands of pigs, beeves, sheep, and the human gland. The prepared proteid shows quite as wide a variation in its iodine content as do the fresh glands. In the following table is given a series of iodine analyses of thyroid glands obtained from healthy animals.

Iodine in Milligrammes Per Gramme of Fresh Gland from Different Species.

Pig.	Sheep.	Beef.	Human.
.084	.006	.030	.060
.120	.013	.040	.080
.300	.016	.103	.094
.300	.016	.165	.200
.648	.018	.168	.216
.710	.018	.187	.316
1.040	.020	.260	.415
1.340	.041	.445	.615
1.470	.214	.610	.814
2.050	.318	.700	
2.88	.415	1.020	
		1.470	

From the above table it is evident that the iodine-content of thyroid glands shows wide variations. Before being used therapeutically it is essential that the proteid should be standardized on the basis of its iodine content, and a uniform intelligent dosage regulated thereby. For the standard we have selected the proteid obtained from normal human thyroid glands.

The average figures of a large number of iodine analyses of the proteid obtained from normal human thyroid glands by the process above described, namely, that of heating the acidified extract to 44° and thoroughly washing the precipitate, is as follows:

ONE GRAMME OF THE PURIFIED PROTEID FROM NORMAL HUMAN THYROID GLANDS CONTAINS 3.384 MILLIGRAMMES OF IODINE.

After the purified proteid from the animal glands is obtained, its iodine content is determined after the method devised by Dr. Riggs, noted above, and regardless of whether this proteid is richer or poorer in iodine than the standard, it is considered that each 3.384 mgms. of iodine represent one gramme of the active thyroid proteid. For the purpose of therapeutic administration the proteid is diluted with the appropriate amount of lactose and made up into two-grain tablets by the usual method. Tablets of different strengths are prepared; 1 per cent., 2 per cent., and 5 per cent. tablets have been found to give a sufficiently wide variation in strength to answer

all the usual requirements. By 1 per cent. tablet is meant that 1 per cent. of the dried weight of the tablet is made up of the purified thyroid proteid according to the standard above described. This may seem to be a very small dose, but our experience proves to us that many patients cannot take a stronger tablet than this. The 1 and 2 per cent. tablets are used almost entirely in the treatment of various types of goitre, some of them being of the atypical exophthalmic variety. It is well known that these patients cannot stand heavy dosing with thyroid proteid. The stronger 5 per cent. tablets are reserved almost exclusively for different metabolic disorders, such as various skin lesions or joint conditions, myxœdema, cretinism, or those conditions in which there is a markedly deficient thyroid activity. It will be observed that by the method of standardizing and preparing the proteids for therapeutic administration, a uniform physiological activity may be expected, regardless of the character of the glands from which the proteid was obtained. A 5 per cent. tablet always contains the same quantity of iodine whether the proteid from which it was made comes from a pig gland containing a relatively high quantity of iodine or from a sheep gland containing a relatively low quantity of iodine. For some purposes it has been found advisable to administer the proteid hypodermatically and, accordingly, solutions of the proteid in varying strengths, standardized on the iodine basis, have been put up in sealed glass tubes. The products prepared according to the method here outlined have been in use for about two and a half years. They have been employed in a wide variety of clinical conditions by a considerable number of experienced clinicians, and the results have demonstrated their value to such an extent that I have no hesitation in saying that this method of preparing and standardizing thyroid is superior to any method now in vogue, that it gives all of the physiologically active portions of the gland, that it contains none of the toxic, deleterious substances contained in the whole extract. In my judgment there is no reason for supplying the wide variety of thyroid preparations which now appear upon the market. The methods described above give everything that is necessary in such form that every therapeutic need is satisfied.

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ANTI-NARCOTIC LEGISLATION.*

By Samuel M. Clement, Jr.

I consider it a great honor to be invited by the Philadelphia College of Pharmacy to discuss with your professors and your students the interesting question of the Law of Narcotics. I have been intensely interested with this subject for the past year, and I realize how important the subject is, not only to pharmacists and physicians, but to the entire community; for, in the time that I have been working with the State Pharmaceutical Board and my friend Dr. Christopher Koch, I have been amazed at the evils to the community resulting from the misuse of narcotics.

It will be interesting to note that the first legislation enacted on the subject of narcotics in the United States was in the Tariff Bill of July 14, 1832, when opium was permitted to be imported to this country without duty; and each succeeding tariff law permitted the free entry of opium, until the Tariff Act of August 30, 1842, was passed, and for the first time a duty varying from 75 cents to $2.50 per pound was placed on opium. This continued until October 1, 1890, when the Tariff Law again placed opium on the free list, where it remained until July 24, 1897, when the Tariff Law of that year placed a duty of $1.00 a pound on opium. It was in 1850 that it was discovered that the Chinese of the Pacific coast were smoking large quantities of opium, and a few years after that the lower classes of the whites and negroes took to smoking opium; so that

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a special schedule on opium used for smoking was placed in the Tariff Act of July 14, 1862, and put on it a tax of 80 per cent. *ad valorem.*

It was considered at that time by those interested in discouraging the smoking of opium, realizing what a deleterious effect it would have on those addicted to its use, that a large duty was advisable, believing that it would prevent its importation; but it soon became apparent that the use of the drug was becoming prevalent and that the quantities brought into this country did not diminish, but increased; this due to the fact that it was being smuggled into this country in very large quantities.

In the Tariff Act of June 30, 1864, in a special schedule, on opium used for smoking a duty of 100 per cent. *ad valorem* was placed; but this did not have the desired effect of preventing the importation of opium. The Tariff Act of July 14, 1870, placed a rate of $6.00 a pound on opium used for smoking, and the Tariff Act of March 3, 1883, again increased it to $10.00 a pound. On October 1, 1890. the Tariff Bill made a further increase to $12.00 a pound. It seemed, however, that the more duty was placed on opium, the smaller were the Custom returns and a larger amount of opium smuggled into the country; so that the tax on opium failed to have any effect in diminishing its general use, and the Dingley Tariff Bill of July 24, 1897, reduced the duty to $6.00 a pound. The next general legislation on the subject of opium was the National Food and Drugs Act of June 30, 1906, which made it mandatory for every one to declare the presence and quantity of opium contained in any article, either used as a medicine or used for food, or which contained any of the derivatives of opium. On February 9, 1909, Congress passed an Act absolutely forbidding the importation of smoking opium and making the possession of it a crime punishable by imprisonment. The wisdom of this legislation will become apparent as we review the general subject further on, because the members of Congress at last realized that smoking opium and the derivatives of opium are the worst menace to the human race that could possibly be imagined. The Tariff Act of 1909 put a duty on crude or medicinal opium containing 9 per cent. or over of morphine of $1.50 a pound, and under 9 per cent. $6.00 a pound. From 1860 to 1890 the tariff on morphine varied from $1.00 to $2.50 per ounce, and from 1891 to 1897 the duty on morphine was 50 cents an ounce; but, after 1897, it became $1.00 an ounce and in 1909 it became $1.50

per ounce. Prior to 1898 cocoa leaves and cocaine were admitted free of duty, but the alkaloid bore a duty of 25 per cent. *ad valorem* up to 1909. The Tariff Bill of 1909 placed a duty of five cents per pound on cocoa leaves and of \$1.50 per ounce on cocaine. The General Appropriation Bill passed May 27, 1908, fixing the appropriation for the Post Office Department of the United States, contained the following words:

"No part of the appropriation herein made shall be used for the carrying in the mails of any malt, vinous, or intoxicating liquors, or intoxicating liquors of any kind; or any cocaine or derivative thereof."

It is interesting to note that on February 26, 1909, The American Association for the Advancement of Science on National Health passed the following resolution:

"We favor a prohibitory tariff, internal revenue tax, and other means which will restrict the use of cocaine, its substitutes and derivatives, to medical purposes."

The revised penal laws of the United States, which took effect January 1, 1910, and which were compiled under the direction of one of the Congressmen from our own State, the Hon. R. O. Moon, gave the Postmaster-General of the United States the power to prevent the passage of cocaine through the mails.

With these thoughts on the national legislation, let us turn our attention to what has been done in the way of legislation on the subject of narcotics by the various States. Forty-five States have passed legislation prohibiting the sale of cocaine except when sold under the prescription of a doctor. Twenty-four of the States regulate the sale of opium and its derivatives, and thirteen restrict the sale of chloral. There are three States that have not, as yet, passed any legislation on the subject of narcotics. A few States—and I am proud to say Pennsylvania is one—make it a crime to have cocaine in your possession.

With this great variance between the laws of the various States and the laws of the national government, let us consider for a moment in what a chaotic condition is this general subject, so important to the welfare of the citizens of our great country. Dr. Hamilton Wright, who has been placed by President Taft in a position of

authority in connection with the Department of State for the purpose of investigating the general subject and reporting to the President the result of his investigation, has made a very careful study of the general subject and he has published from time to time statistics that are most interesting and which, I believe, will have the effect of arousing a great public sentiment on this question. Dr. Wright has made a most thorough investigation, and great credit is due to him and the Department of State for what he has already accomplished. We find from Dr. Wright's statistics that, during the period from 1860 to 1869, there was imported into the United States 1,425,196 pounds of opium of all forms, and, during the period from 1900 to 1909, there was imported 6,435,623 pounds of opium. This, you will see, is an increase of 351 per cent. of opium imported into this country, while the population of the country during the same periods shows only an increase of 133 per cent. There are in the United States to-day about 120,000 Chinese, 35 per cent. of whom smoke about 100,000 pounds every year. As I said a few moments ago, it was discovered in 1860 that smoking opium had been adopted by the lower classes of the whites and negroes of this country, and this has grown so that we are told to-day that there are about 150,000 Americans who smoke annually about 68,000 pounds of opium. We frequently find, especially along the Pacific coast, white women who are living with Chinamen and smoking opium.

It will be interesting to note, by way of comparison, what effect opium has on the other countries. Italy, with a population of about 33,000,000, imports and uses but 6000 pounds of opium. Austria-Hungary, with a population of about 46,000,000, uses between 3000 and 4000 pounds of opium. Germany, with a population of about 60,000,000, uses about 17,000 pounds of opium a year, and Holland, with a population of about 6,000,000, imports and uses but 3000 pounds per annum. To the credit of all of these old countries, it can be said that they have the strictest laws regulating the sale of habit-forming drugs.

It is appalling when we consider that in the United States with a population of about 90,000,000 people, we consume the enormous quantity of over 400,000 pounds of opium every year—more than all the other countries I have mentioned put together. It has been conservatively estimated that only 25 per cent. of this enormous amount can find any legitimate use and that the balance of 300,000

pounds is used by the fiends, either in the form of smoking or by using morphine. It is said that 80 per cent. of the 400,000 pounds used in this country is used in the manufacture of morphine and that about 75 per cent. of morphine made in the United States is used by dope fiends. It will be interesting to know that these dope fiends are divided as follows:

Six per cent. of all the persons entering our large penal institutions have been found to be addicted to the opium habit in some form, and of the general criminal population of this country 45.48 per cent. are habitues of opium, morphine, or cocaine; 21.6 per cent. of the lewd women of this country and their hangers-on are also addicted to the drugs; 2.06 per cent. of the medical profession of this country are addicted to drugs; 1.32 per cent. of the trained nurses of this country are addicted to drugs; .684 per cent. of other professions are addicted and .18 per cent. of our adult population, outside of those enumerated, are addicted to opium or its derivatives.

We find that outside of the large cities, even into the country districts, the use of opium and its derivatives has increased tremendously. One hundred and fifty thousand ounces of cocaine are manufactured annually in the United States, of which about 135,000 ounces go to make demons out of human beings. Cocaine is without exception the most dangerous drug known to society. It is seductive in character and produces a sense of keen exhilaration and exaggerated power. It completely wrecks the individual and makes a dangerous criminal of him. A man or woman charged with cocaine will commit any crime or stoop to the lowest and most immortal acts. Most of the crimes committed by the Southern negroes are the result of coke-charged brains. It has been found that the cocaine habit is becoming very prevalent among the negro race, not only the negroes of the South, but the negroes of our own city and other cities of the North, and it has been found that in certain low dives in the South much of the whiskey sold is doctored with cocaine.

It has been said that the cocaine habit is essentially American; but do not let us think for a moment that it is confined entirely to the lower classes. In fact, it has invaded the higher ranks of the so-called society of our country, and it is astounding to find how general is its use among those who consider themselves the great social leaders of the country. Cocaine has invaded even the ranks of the Army and the Navy, and I regret to say that it has even

been found in the school-room; for in our own city we found schoolchildren buying cocaine from negroes in five and ten cent packages.

These statements are made with the idea of arousing a sentiment on this general subject; for, if it is not checked, no one can tell to what extent the evil is going to affect this country and its people.

It is known that the drug habit is a sort of a secret habit and all people who use drugs do so with the greatest secrecy. The best step that can be taken is to eliminate the secrecy as much as possible, and I desire to express my appreciation to the newspapers of Pennsylvania for having given the general crusade against cocaine so much publicity; for I know of nothing that will help to eliminate this terrible habit among our people more than publicity.

There should be an agreement between nations so that smuggling of opium will be impossible; secondly, we should have a Federal law to control the interstate traffic; and, third, we should have a uniform interstate law; because, of course, the national government can only control interstate commerce, but cannot control interstate trade. Next we must have laws that will be far-reaching and will carry with them severe punishments, and we must have eternal vigilance and honest, capable, trustworthy officials to enforce the law. At this time I desire to express my great appreciation for the noble work done in hunting out the sellers of opium and cocaine by the Department of Public Safety of Philadelphia. The Director of that Department and his assistants have been untiring in their efforts to co-operate with the State Pharmaceutical Board, and the records of the Court of Quarter Sessions of Philadelphia County will show that a great many of them have been punished and a great many more are still to be punished when the cases are tried.

President Taft has appointed delegates to the International Opium Congress, and we believe that an international agreement will be the result.

In framing legislation we should remember that drug fiends are largely the victims of circumstances and are more to be pitied than censured; but the careless physician who prescribes cocaine or morphine, or the careless pharmacist who refills prescriptions for cocaine and morphine, are the ones who should be severely dealt with, and the sale of patent and proprietary remedies doped with morphine and cocaine should be prohibited and the manufacturers should be severely punished, for we find proprietary remedies

recommended, for infants as well as adults, containing morphine and cocaine, and many a dope fiend to-day can properly charge the forming of that habit to the taking of morphine when a child, in patent medicines.

As I said a moment ago, the Federal government cannot prohibit the use of cocaine or morphine in the States; all it can do is to regulate interstate commerce with respect to it and prohibit importation, which will be done. The duty rests upon each individual State, however, to pass legislation which will be uniform, so that there will be no question of jurisdiction; so that there will be no question of one State prohibiting cocaine and another one permitting it. Pennsylvania has taken the lead in the legislation with reference to cocaine and morphine, and the officials of Pennsylvania, both State and municipal, have demonstrated that this evil can be dealt with successfully.

The following are some of the essential features of Hamilton Wright's Interstate Bill:

First: "That such an Act should demand the registration of every person who imports, produces, manufactures, compounds, distributes, or otherwise handles habit-forming drugs in interstate or foreign commerce.

Second: "That importers, wholesale compounding pharmacists, and wholesale dealers should pay a small per-annum tax of $10, and that retail pharmacists and other retail dealers, including physicians who buy in interstate commerce and who carry large supplies of the drugs, should pay a tax of from $1 to $3 per annum; that every one engaged in handling drugs should register and pay a tax."

Third: "That, without attempting to derive a revenue beyond the amount necessary to administer the act, all of the habit-forming drugs should have imposed upon them an internal-revenue tax of 1 cent an ounce, and that such tax should be paid by affixing to packages or other receptacles containing the drugs, an engraved stamp, to be affixed and cancelled according to law."

Fourth: "That all compounds or preparations manufactured from the original tax-paid drugs should be marked or branded in such a manner as to show the payment of the tax on the original drug."

Fifth: "That every person concerned in the importation, manufacture, remanufacture or compounding, selling or dispensing of habit-forming drugs and their preparation, should keep such books, render such returns, and give such bonds as may be determined by the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury."

Sixth: "That it should be unlawful for any person to sell, give away or otherwise dispose of in Interstate Commerce, any of the habit-forming drugs, their salts, derivatives, or preparations to any person other than a person who has registered and paid the special tax, public hospitals and scientific and public institutions excepted."

Seventh: "That all of such drugs, their derivatives and preparations imported should pay an internal-revenue tax equal to that imposed on the home-produced drugs."

Eighth: "That on trial for violation of such an act, illegal possession of such drugs should be deemed as sufficient evidence of such violation, unless the defendant shall explain the possession to the satisfaction of the jury."

Ninth: "That all returns required by such an Act should be filed and recorded in the office of the Commissioner of Internal Revenue, under such regulations as may be approved by the Secretary of the Treasury, and that these returns should be open to the inspection and certified copies should be made to the proper officials of any State, territory, or district under the jurisdiction of the United States who are charged with the enforcement of local laws regulating the prescribing, dispensing, sale, or use of such drugs."

Tenth: "That heavy penalties, either by fine or imprisonment, or both, should be imposed on the violator of such an Act."

By making this a revenue measure, it is placed in charge of the Treasury Department and that Department has a well-trained corps of collectors and secret service men, who could see to the proper enforcement of the Act.

I should like at this time to read to you a few thoughts with reference to legislation in the State of Pennsylvania that it would be well for you to consider, and I am also delighted to say to you that Senator James P. McNichol has promised me that he will father the legislation in the next House and Senate for the regulation

and sale of cocaine and morphine and will insist upon the severest penalties being placed in the Act, so that all those that we have been discussing who violate the law can be properly dealt with.

The following outline is suggested for a State Anti-Narcotic Law:

Cocaine, Eucaine, and Other Synthetic Substitutes, Their Derivatives, Salts, and Compounds.

1. Sold only on prescription of a registered physician, a dentist, or a veterinarian, which is not to be renewed or copied and must be kept on a separate file for five years, and a veterinarian shall not prescribe for human beings.

2. Wholesale druggists can sell to retail druggists, other wholesale druggist, or manufacturer of same article.

3. Manufacturers can sell to other manufacturers of same article or to wholesale druggists.

4. Manufacturers, wholesale druggists, and retail druggists shall keep accurate records of all sales and use of all cocaine, etc.

5. Manufacturers, wholesale druggists and retail druggists shall make monthly reports to the body or commission entrusted with the enforcement of the law, showing all sales and other uses to which it has been put.

6. Illegal possession a crime.

7. Prescription files and records subject to inspection of proper officers.

8. Severe penalties of imprisonment.

Morphine, Opium, or Their Derivatives or Compounds.

1. Sold only on prescription of registered physician, dentist, or veterinarian, which is not to be renewed or copied and to be kept on a separate file for five years. A veterinarian shall not prescribe for human beings.

2. Wholesale druggists can sell to other wholesale druggists, or manufacturers of same article or to a retail druggist.

3. Manufacturers can sell to other manufacturers of the same article, wholesale druggists, or retail druggists.

4. Manufacturers, wholesale druggists, and retail druggists shall keep accurate record of all sales and use of all morphine, opium, its salts, derivatives, and compounds.

5. Manufacturers, wholesale druggists, and retail druggists shall make monthly reports to the body or commission entrusted with the

enforcement of the law, showing all sales and other uses to which it has been put.

6. A physician may prescribe but not dispense these drugs to habitual users under treatment, provided he keeps a record of the patient, together with the name and quantity of drug prescribed, and reports the same in monthly reports to the body or commission enforcing the law.

7. Illegal possession a crime.

8. Prescription files and records subject to inspection of proper officers.

9. Severe penalties of imprisonment.

The Act not to apply to cough remedies, proprietary medicines, or other medical preparations sold as medicines and not for the purpose of evading the provisions of this Act or supplying habitues with the drug if they contain not over (to the ounce)

2 grains of opium,
¼ grain of morphine,
¼ grain of heroin,
¾ grain of codeine.

(Or not more of any other derivative or compound of same.)

Providing the quantities of the drugs contained shall be plainly stated upon the label.

Also providing that any preparation intended for soothing syrups for infants shall not contain any of the drugs.

Also providing that regular practising physicians can supply the drugs, providing they comply with the other provisions of this Act of Assembly with reference to reporting and keeping a record.

And providing that prescriptions or orders for plasters, liniments, and ointments when intended for external use only, and when the quantity of the drug is plainly marked on the label, shall be permitted.

In conclusion, permit me to say that I believe that if laws such as these were passed by the national government, and the different States of this Union, there is no reason why the Narcotic Laws of the country should not then be effective; but even with the best of legislation, we should always remember that " eternal vigilance is the price of liberty;" and I know of no better means of keeping this agitation before the State than through the columns of the news-

papers of Pennsylvania. It is true that it may be said that these laws will be a little burdensome for the pharmacists; but they should remember that the laws are for the protection of their brother man and that they should be willing to bear part of the burden, for if the pharmaceutical profession should not be willing to assume its share and assist in the passage of some practical law, it is more than likely that some others, not acquainted with the pharmaceutical profession, might attempt to draw and pass impractical and oppressive laws; for it can be said with certainty that the sale and consumption of habit-forming drugs will be controlled in this great country of ours.

ABSTRACTS OF SOME OF THE PAPERS PRESENTED TO THE PENNSYLVANIA AND NEW JERSEY STATE PHARMACEUTICAL ASSOCIATIONS.

By John K. Thum, Ph.G.,
Pharmacist at the German Hospital, Philadelphia.

Unguentum Resorcini Compositum.—By William Dulin, Penn. Pharm. Assoc.

After some experimentation with this ointment the author arrives at the conclusion that the water in the hydrous wool-fat is the cause of the discoloration which manifests itself after the ointment has been made some time; the water dissolving the resorcin, which in turn exerts some action on the oil of cade. To overcome this tendency he recommends that the hydrous wool-fat be replaced by the anhydrous.

Asafetida.—By W. H. Pearson, Penn. Pharm. Assoc.

When the Food and Drugs Act first went into effect there was considerable improvement in the quality of asafetida imported to this country, but after a few lots of inferior quality failed to be deported, European merchants declared that the best grades were unobtainable in sufficient quantity. The author states that the motive underlying this plea was to influence the Revision Committee of the Pharmacopœia to adopt lower standards.

He also states that it is difficult to get representative samples of this gum and illustrates as follows: " A sample consisting of several lumps was pounded in an iron mortar till fairly uniform and the

ash amounted to 24.9 per cent., the alcohol soluble to 50.86 per cent. The same case was later resampled and the average of four results obtained indicated 54.5 per cent. of ash and only 23.2 per cent. of alcohol soluble material, almost the reverse of the results formerly obtained."

To determine the per cent. of alcohol soluble material he puts 10 grammes of the sample and 150 c.c. of alcohol in a mechanical shaker for several hours, collecting the insoluble portion on weighed filter paper, washes well with an excess of alcohol, and dries to constant weight at 100° C.

Theoretically, he says, powdered asafetida should be of the same standard as the whole gum, but it is not convenient because of the moisture and volatile material that is present. If dried before powdering much volatile material is lost. He shows the loss of asafetida during the drying and powdering of four different lots, the average loss being 20.25 per cent., the loss being nearly all of the volatile and alcohol soluble portion, and this loss, he states, increases the ash and alcohol insoluble material in the finished product.

He also says that the results of investigation of powdered samples do not vary so much as samples of the gum because of the powder's comparative uniformity.

A definite standard for the amount of soluble material in the tincture should be insisted upon, he states in closing.

TINCTURA OPII CAMPHORATA.—By WILBUR F. HORN, Penn. Pharm. Assoc.

The author is of the opinion that substituting an equivalent amount of the tincture of opium for the opium present in the official formula for camphorated tincture of opium possesses distinct advantages, such as facility of manufacture and saving of time.

A METHOD OF ASSAYING THE OINTMENT OF MERCURIC NITRATE, U.S.P.—By I. V. STANISLAUS and E. ARTHUR EATON, Penn. Pharm. Assoc.

Stating that they were unable to find any assay for this ointment in either standard text-books or journals, the authors proceed to give a method of their own which, they remark, is accurate within about 0.13 per cent.

"About 3 grammes of the ointment were weighed in a beaker

and 3 grammes of potassium hydroxide, dissolved in 35 c.c. of water, added. This was then heated upon the water-bath until saponification was complete and allowed to stand for from 24 to 48 hours, to allow the separation of the mercuric oxides. The mixture was then filtered (the filtrate being reserved to ascertain if any further deposit occurred). The precipitate was then washed well and transferred, paper and all, to an Erlenmeyer flask and 50 c.c. of nitrohydrochloric acid added. The flask and contents were shaken occasionally until solution was complete. The solution was then diluted with 50 c.c. of water and the paper pulp filtered off and washed well. The filtrate was then evaporated to dryness in capsule, and the residue of mercuric chloride taken up with 100 c.c. of water and dissolved by the aid of heat. Hydrogen sulphide gas was next passed in until saturation; the precipitated mercuric sulphide filtered off and washed. Next, the precipitate, paper and all, was transferred to a glass-stoppered bottle, an excess 30 c.c. of $\frac{N}{10}$ iodine solution added and 5 c.c. of carbon disulphide. The bottle was shaken for five minutes and allowed to stand for half an hour. Then the excess of iodine was titrated with $\frac{N}{10}$ sodium thiosulphate solution."

Some Formulas for Elixirs Proposed for Recognition in the Revision of the National Formulary.

George M. Beringer, N. J. Pharm. Assn., offers some formulas for elixirs to be included in the next revision of the N.F. with the hope that they be tried and criticized by practical pharmacists.

In speaking of elixir of calcium lactophosphate the author states that as the salt is now commercially obtainable a definite weight of it should be directed to be dissolved in aromatic elixir. The following formula is suggested:

Calcium lactophosphate	25.0 Gm.
Lactic acid	8.0 c.c.
Aromatic elixir to make	1000.0 c.c.

The present National Formulary formula for elixir of glycerophosphates is deficient in flavoring as it contains only 300 c.c. of aromatic elixir. He modifies the formula and adds a requisite amount of compound spirit of orange. Lactic acid is used instead of phosphoric acid as it seems to be more effective in preventing precipitation of these salts. The modified formula is as follows:

Elixir Glycerophosphatum.

Sodium glycerophosphate (75 per cent.)	22 Gm.
Calcium glycerophosphate	8 Gm.
Lactic acid	8 c.c.
Glycerin	300 c.c.
Compound spirit of orange	12 c.c.
Alcohol	125 c.c.
Purified talc	15 Gm.
Distilled water, sufficient quantity to make..	1000 c.c.

The author also recommends that the next revised National Formulary contain a compound elixir of the various glycerophosphates and advises the inclusion in this book of the following formula:

Elixir Glycerophosphatum Compositum.

Sodium glycerophosphate (75 per cent.).	44	Gm.
Calcium glycerophosphate	16	Gm.
Iron glycerophosphate	3	Gm.
Manganese glycerophosphate	3	Gm.
Quinine glycerophosphate	1	Gm.
Strychnine glycerophosphate	0.125	Gm.
Lactic acid	8	c.c.
Compound spirit of cardamom	10	c.c.
Alcohol	125	c.c.
Glycerin	350	c.c.
Purified talc	15	Gm.
Distilled water, sufficient quantity to make	1000	c.c.

As the formates have within recent years become exceedingly popular abroad, and as the British Pharmaceutical Codex has included formulas for elixirs and a syrup, which indicates more or less use in the British Islands, he advises the introduction of the following formulas:

Elixir Formatum.

Potassium formate	50 Gm.
Sodium formate	50 Gm.
Aromatic elixir, sufficient quantity to make..	1000 c.c.

Elixir Formatum Compositum.

Sodium formate	32	Gm.
Magnesium formate	16	Gm.
Strontium formate	30	Gm.
Lithium formate	7.5	Gm.
Quinine formate	7.5	Gm.
Formic acid	10	c.c.
Compound spirit of orange	10	c.c.
Acetic ether	1	c.c.
Alcohol	100	c.c.
Glycerin	300	c.c.
Purified talc	20	Gm.
Distilled water, sufficient quantity to make	1000	c.c.

The Compound Spirit of Cardamom

called for in these formulas is as follows:

Oil cardamom	20	c.c.
Oil clove	1	c.c.
Oil cassia	2	c.c.
Oil orange	20	c.c.
Oil caraway	0.1	c.c.
Anethol	1	c.c.
Alcohol, to make	200	c.c.

The Need for the Practical Pharmacist in Pharmacopœial Revision.

George M. Beringer, N. J. Pharm. Assoc., makes the statement that the development and progress made by the profession of pharmacy as a separate branch of medicine accounts for the increasing influence of pharmacists in the matter of pharmacopœial revision the last several decades.

Physicians comprising the Revision Committee elected by the Convention of 1840 realized the value of practical pharmacists, asked for such aid as was needed by them in revising this book, and were grateful and quick to acknowledge their indebtedness. Following the 1840 Convention, delegates from schools of pharmacy and pharmaceutical societies have worked together to revise and produce an acceptable national standard. He then goes on to say

that there is as much need now in the revision of this book for the experience and practical knowledge of the pharmacist as ever before. Formulas for the various preparations should be practical; correct, both as to quantities and ingredients; and should be workable on a small scale in the average retail pharmacist's laboratory as well as on a large scale in that of the manufacturer.

The Pharmacopœia, he says in closing, can only be improved and brought nearer to our ideal of perfection by each one fully discharging his duty in connection therewith. The pharmacist has his share of the responsibility. He should test the formulas, report errors found in the book, and suggest improvements and better methods for exhibiting some of the remedies.

THE PHARMACEUTICAL INSTITUTE OF THE UNIVERSITY OF BERLIN.*

By M. I. WILBERT, Washington, D. C.

As a contribution to the Centenary of the University of Berlin, which was celebrated in the early fall of 1910, the director of the Pharmaceutical Institute has compiled the story of the origin and evolution of the course in pharmacy at this University, from its foundation in 1810 to the year 1910.

The resulting, rather ornate, volume of 134 oblong pages also embodies a description of the present Institute illustrated by upwards of 48 photographic reproductions and diagrams.

This latter portion of the book is particularly interesting to American readers because it serves to reflect, in a way not commonly met with, the thoroughness and completeness of the courses in pharmaceutical instruction that are offered in connection with German universities. It also illustrates the need for assisting pharmaceutical schools by liberal endowments or material contributions from the general education fund, if pharmacy is to hold its own as a professional calling and is to continue to take an active part in the development of the sciences that are involved.

The University of Berlin has been particularly fortunate in

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* The frontispiece in this issue, to illustrate this article, was made after a photograph which Professor Thoms, Director of the Pharmaceutical Institute of the University of Berlin, kindly sent to the editor of this JOURNAL.—EDITOR.

its selection of men as teachers in the sciences related to pharmacy. The teachers who have assisted in developing the course of pharmacy at this university include men whose names are widely known and who are generally recognized as having been active in the development of the several sciences in which they were specialists.

The first teacher in chemistry was Martin Heinrich Klaproth (1743–1813) who is generally recognized as being second only to the immortal Scheele in practical contributions to the pharmaceutical chemistry of his day. One of his younger contemporaries was Sigismund Friedr. Hermbstätt (1760–1833) a practical pharmacist who taught chemistry and pharmacy and also contributed many articles on pharmaceutical-chemical subjects to the literature of his time.

One of the successors to Klaproth was Eilhard Mitscherlich (1794–1863) a student and associate of the great Berzelius and the discoverer of a number of now well-known chemical compounds, among others, of permanganic acid and its salts. Associated with Mitscherlich were such well-known men as Heinrich Rose (1795–1864) a teacher as well as an investigator, Friedr. Wöhler (1800–1882) later the associate and successor of Liebig at Giessen, H. G. Magnus (1802–1870) and Gustav Rose (1798–1873).

Among the later teachers of chemistry were such well-known men as E. R. Schneider, A. W. Hofmann, Adolf Baeyer, Adolf Pinner, Emil Fischer, and the present director of the Institute, Dr. Hermann Thoms.

The list of teachers of physics include such well-known names as Dove, Magnus, v. Helmholtz, Kundt and Wehnelt.

In botany Heinr. Friedr. Link (1765–1851) was followed in 1851 by Alexander Braun who had as associates O. C. Berg, C. H. E. Koch and N. Pringsheim, all men who were able to leave their imprint on the progress of botany and pharmacognosy. Among the later teachers of botany and pharmacognosy we find such well-known names as Karsten, Garcke, Eichler, Schacht and Engler.

These all too limited references will serve to demonstrate that the century of pharmaceutical instruction at the University of Berlin has been one of promise and possibilities despite the fact that for upwards of 90 years the course was severely handicapped by hopelessly inadequate facilities for laboratory instruction and even deficient provision for lectures and demonstrations.

The present status of the Pharmaceutical Institute of the University of Berlin, on the other hand, is an excellent illustration of the benefits that may and do accrue to the community at large by fostering independent pharmaceutical laboratories and liberal pharmaceutical training.

In connection with the reviews of the annual reports of the Pharmaceutical Institute of the University of Berlin that have been published in this JOURNAL, attention has been called to some of the various activities of the Institute. Not the least valuable of the work now done, from the viewpoint of the public health, is the exposing of secret or proprietary remedies that has been undertaken at the request and with the assistance of the German Society of Apothecaries.

The work that has been done in connection with new remedies is also of importance, while the original chemical and phytochemical investigations that have been reported have attracted widespread attention and have contributed much to pave the way for securing to pharmacy the recognition that the calling properly deserves.

Altogether it may be pointed out that the Pharmaceutical Institute, as now constituted, bids fair to be an active factor in bringing about a realization of the possibilities outlined by Flückiger, nearly thirty years ago, in recommending the practical elaboration of the courses of pharmacy in connection with German Universities.

In his recommendation, reproduced by Thoms in the volume under discussion, Flückiger points out that many of the problems relating to the preservation of the public health can and should be solved by pharmacists.

He further points out that if pharmacists were given the necessary training partially or wholly at the expense of the State they in turn would be in position to assist, in a practical way, in improving the hygienic conditions of the communities in which they reside.

As intimated above it is only in very recent years that the authorities, recognizing the possibilities of practical returns, saw fit to provide the necessary facilities for laboratory investigations and original research that are embodied in the evidently well equipped and truly magnificent institute at Dahlen adjoining the grounds of the Botanical Garden of the University of Berlin.

For us in America the excellent work that is being done for

the public welfare in the Pharmaceutical Institute of the University of Berlin should be both an inspiration and a promise. An inspiration to emulate the spirit that dominated the men who through the many years of adversity struggled on, despite their inadequate facilities, instilling into their students the scientific spirit that dominated them and their predecessors.

The present elaborately equipped Institute of the University of Berlin is a promise in that it demonstrates that properly directed scientific work will and must be recognized and that pharmacy is assured of a promising future in all parts of the civilized world where its followers are earnestly and honestly laboring for the public good.

CORRESPONDENCE.

THE AMERICAN JOURNAL OF PHARMACY,
145 N. 10th St., Phila., Pa.

GENTLEMEN: The Committee on Standards for Unofficial Drugs and Chemical Products are engaged in formulating standards for a number of articles not now recognized by the U. S. Pharmacopœia. Many of the articles which they are standardizing will, no doubt, be admitted into the Revision of the National Formulary, now in process, and if the standards as promulgated by this Committee are adopted in that revision, then they will become the legal standards of the country.

It has been suggested that a list of the monographs immediately under consideration should be published in the pharmaceutical journals so that the importers, manufacturers and dealers who are interested will feel at liberty to make suggestions as to the proper standards to be adopted. It is the desire of the Committee to be absolutely fair and accurate as far as possible in our work, and we welcome any suggestions that may be offered. The following list of titles covers only those on which monographs are now before the Committee:

Absinthium, Aconite Leaves, Adonis, Albumen (Dried Blood), Albumen (Dried Eggs), Althæa Leaves, Ammonium Hypophosphite, Angelica Root, Angelica Seed, Areca, Arnica Root, Barium Peroxide, Boldo Leaf, Bromauric Acid (Commercial Gold Tribromide), Buckthorn Berries, Cacao (Cocoa), Cactus Grandiflorus, Calamine, Calcium Glycerophosphate, Calcium Peroxide, Canella Alba, Cas-

carilla, Caulophyllum, Celery Seed, Centaury, Coal Tar, Cocculus Indicus, Condurango, Coto Bark, Cudbear, Diacetyl Morphine, Diacetyl Morphine Hydrochloride, Dextrin (White), Dextrin (Yellow), Euphorbia Pilulifera, Foenugreek, Formic Acid, Formic Acid (Concentrated), Kava Kava, Kieselguhr, Kola, Lead Carbonate, Oil Cardamom, Phenolphthalein, Poppy Capsules, Potassium Glycerophosphate, Quince Seed, Red Gum (Eucalyptus), Kino, Rennin, Saffron, Sherry Wine, Strontium Arsenite, Thuja (Arbor Vitæ), Tonka Bean, Venice Turpentine, White Pine Bark, Zinc Peroxide.

It is the intent to publish, from time to time, supplemental lists as new articles are taken up for standardization. In order to give the desired publicity to our work, we respectfully request the pharmaceutical press to give sufficient space to present this matter and request that any suggestions as to the proper standards to be adopted should be sent to the undersigned.

Yours respectfully,

George M. Beringer,
Chairman.

501 Federal St., Camden, N. J.

BOOK REVIEWS.

Pharmacopœia Nederlandica, Edito Quarta, Supplenda et Mutanda I. Amstelodami mcmx. This, the first instalment of additions and corrections to the fourth edition of the Netherlands Pharmacopœia, published in 1905, comprises an octavo pamphlet of approximately 55 pages the same shape and size as the pharmacopœia published 5 years ago.

The book or pamphlet is published by the standing pharmacopœia commission and like the Netherlands Pharmacopœia itself is available in both a Dutch and a Latin edition.

The new additions number 14 and include, Acidum acetylosalicylicum, Acidum diaethylobarbituricum, Amylum Manihot, Antipyrinum cum Coffeino et Acido citrico, Dimethylaminoantipyrinum, Emulsum Olei Iecoris Aselli compositum, Extractum Cola liquidum, Flores Lavandulæ, Hexamethylentetraminum, Semen Cola, Solutio Hydrochloratis Suprarenini, s-Suprareninum, Tannas hydrargyrosus, and Thiosulphas Natricus.

The recognition of suprarenal alkaloid under the general title

s-Suprarininum with adrenalinum as a synonym is rather interesting because of the comparatively small amount of attention that appears to have been given this product on the Continent of Europe. It is also interesting to note that the Dutch title "l-suprarenine" and the final requirement that the product on incineration is to leave no residue would indicate that the synthetic, lævorotatory, product is preferred.

The corrections affect no less than 110 of the official titles and are mainly changes in requirements and tests. All of the changes are important in that they suggest precautions that should be taken in connection with a work of this kind to insure fair and equitable standards and requirements.

In this connection it is interesting to note that in place of making definite fixed requirements for the alkaloid content of drugs and pharmaceutical preparations the Ph. Ndl. IV now permits of a range of standard or a variation of approximately 20 per cent. from the original requirements.

The greater number of changes embodied in this first instalment of corrections are due to an elaboration of the requirements for the specific gravity of liquid preparations, usually a material increase of the permissible variation.

The directions for keeping many of the official drugs and preparations are also somewhat elaborated, particularly in connection with narcotic leaves and herbs which are now directed to be protected from the influence of light.

Apart from the changes mentioned it may be noted that the comprehensive and in many ways elaborate descriptions for organic drugs appear to be satisfactory, only one additional change being embodied in the present list. This change is an increase in the permissible ash content of lupulin from 6 to 10 per cent., making it similar to that of the U.S.P.

The pamphlet, apart from the suggestions on requirements to be avoided or at least interpreted liberally, is a commendation of the care exercised by the Committee of Revision which prepared and published the Netherlands Pharmacopœia of 1905.

M. I. W.

OBITUARY.

LOUIS DOHME.

Louis Dohme, president and one of the founders of the well-known pharmaceutical manufacturing firm of Sharp & Dohme, died at the Union Protestant Infirmary, Baltimore, January 12, after an illness of some weeks, neuritis being the direct cause of his death.

While always applying himself closely to business affairs up until a few years ago, Mr. Dohme was in the habit of going abroad during the summer for rest and recreation. Early in June last he made his annual pilgrimage abroad, spending the most of his time at the baths of Wiesbaden, where he had received benefit on a previous visit. On his return trip, about 9 weeks ago, he was taken ill aboard the steamer, arriving in New York in an unconscious condition. From the steamer he was taken to a sanatorium in New York. Here he remained two weeks, making slight improvement, when he was taken to the Infirmary in Baltimore, where it was soon realized that his condition was serious.

Mr. Dohme was a foreigner by birth, he having been born in Obernkirchen, Germany, on July 6, 1837. His early education was obtained in a private school in his native town. When he was fifteen he and his five brothers and one sister were brought to this country by their parents, the late Charles and Sophia Dohme.

After attending Knapp's School, in Baltimore for several years, young Dohme entered the drug store of the late A. P. Sharp, where he soon gave evidence of those qualities which led to the prominence and success which he attained in the chemical-pharmaceutical manufacturing line. While serving his apprenticeship he attended the Maryland College of Pharmacy, graduating in 1856 with the highest honors. Four years later he was taken into the firm, the name being changed to Sharp & Dohme. The store occupied the corner at Pratt and Howard Streets, a part of the present site of the firm, and one of Mr. Dohme's first moves after the formation of this partnership was to increase the capacity of the building with the object of engaging in the manufacture of pharmaceutical preparations on a small scale. When in 1866 his brother, Charles E. Dohme, was taken into the firm, it was decided to increase still further the laboratory facilities and to engage in the manu-

facture of a general line of preparations. In the division of their labors, Charles E. Dohme took charge of the laboratories and Louis began to introduce their products to neighboring physicians, pharmacists and wholesale druggists, finally extending his territory until it practically covered the United States east of the Rocky Mountains. It is said that Mr. Dohme made many friends among those he visited, and that these have remained as loyal patrons of the firm ever since.

Mr. Sharp withdrew from the firm in 1885, and the next year it was incorporated with Louis Dohme president, Charles E. Dohme vice-president and Ernest Stauffen secretary and treasurer, the latter also having charge at present of the firm's New York office. Besides the officers, C. P. Dohme, a younger brother, and Dr. A. R. L. Dohme were included in the Board of Directors.

Mr. Dohme was not alone interested in seeing his firm advance, but was active in advancing the cause of pharmacy in other ways, he having held several positions of honor and trust. For some years he was chairman of the Board of Examiners of the Maryland College of Pharmacy and in 1875 was elected president of the College, serving in this position until 1890, when he was succeeded by his brother Charles E. Dohme, who held the position until the affiliation of the College and the University of Maryland. In 1900 he was elected a member of the Board of Trustees of the U. S. Pharmacopœial Convention. He was a member of the Maryland State Pharmaceutical Association and a life member of the American Pharmaceutical Association, and a member of the social clubs, the Germania and Country Clubs of Baltimore. He was fond of art and literature, and devoted much of his spare time to the reading of the classics.

Mr. Dohme was unmarried, and had made his home for the past 25 years with his brother, Charles E. Dohme, at 822 North Carrollton Avenue. His funeral was held here.

He is survived by two brothers—Messrs. Charles E. and William F. Dohme. He also left six nephews—Drs. A. R. L. and Gustavus C. Dohme; Messrs. Justus Dohme, C. Louis Dohme, of Culpeper, Va.; William I. F. Dohme, of Montclair, N. J., and Carl A. G. Frisius—and six nieces—Misses Adele C. Dohme, Clara Dohme, Nettie Dohme, of Montclair, N. J.; Mrs. Charles G. Holzhauer, of Newark, N. J.; Mrs. Alma Von Marees and Miss Agnes Frisius.

A portrait of Louis Dohme is given in the frontispiece of the

June, 1910, issue of this JOURNAL, as one of the members of the Board of Trustees of the U. S. Pharmacopœial Convention of 1890.

PHILADELPHIA COLLEGE OF PHARMACY.

MINUTES OF THE QUARTERLY MEETING.

The quarterly meeting of the College was held on December 27th, 1910, at 4 P.M. in the Library. Eleven members were present. The President, Howard B. French, presided. The minutes of the semi-annual meeting held September 26, were read and approved. The minutes of the Board of Trustees for September, October, and November, were read by the Registrar, and approved.

The President appointed the following members as the Permanent Committee on Centenary Celebration of the College, George M. Beringer, Chairman, Joseph P. Remington, Henry Kræmer, Samuel P. Sadtler and M. I. Wilbert; and on the Committee on Legislation, Joseph P. Remington, Chairman, M. I. Wilbert, William McIntyre, Warren H. Poley, Theodore Campbell and Charles Leedom. Professor C. B. Lowe presented through J. M. Maris & Co. a small ground stopper bottle which was formerly used in the store of the late Charles A. Heinitsh, of Lancaster, and said to be one hundred and thirty years old. The thanks of the College were tendered the donor.

The President appointed Joseph W. England, George M. Beringer, and Joseph P. Remington a committee to draft suitable resolutions on the death of Professor Hallberg, and to report to the meeting of the Board of Trustees to be held on January 3, 1911.

ABSTRACT FROM THE MINUTES OF THE BOARD OF TRUSTEES.

September 6, 1910. Sixteen members present. Mr. Wallace Procter, an ex-member, was also present. The Committee on Announcement reported the issue of Bulletin No. 4, Vol. 2; also that a Spanish edition of the Bulletin was being prepared.

Mr. French read a communication from the executors of the estate of Robert W. Johnson, relative to the legacy left by him to

the College. He also read the bond necessary to be filled out, upon receipt of which the legacy would be paid.

Mr. England read several communications relative to the mailing of periodicals issued by the College, which were referred to the Committee on Publication for their consideration, and to be reported on to the College.

Mr. Cliffe read a communication relative to entrance examinations, which was referred to the Committee on Instruction.

October 4, 1910. Fourteen members present. The Committee on Property reported the changes made in the Pharmaceutical Laboratory and on the fifth floor, the latter giving a suitable room for physical training. Mr. Cliffe reported that the Director, Dr. Schleif, and Instructor, Mr. Beam, considered the room well lighted and ventilated, and when equipped would prove one of the best gymnasiums in the city.

Committee on Library reported, Librarian, Miss Katharine E. Nagle in charge, and the Committee on Examinations reported that James Henry Allen, Frank Earl Haines, and Miss Aase Teisen had satisfactorily passed all examinations in the Course for the Certificate of Proficiency in Chemistry, and that Peter Amsterdam had satisfactorily passed the examination for the Certificate of Proficiency in the Food and Drug Course; and these certificates were accordingly awarded.

Committee on Announcement reported that the Special Bulletin relating to the course of instruction in Analytical Chemistry and Food and Drugs course was in press, and that the Spanish edition was being printed.

Committee on Commencement reported that the Academy of Music had been leased for May 25, 1911.

Committee on Scholarships recommended the names of eleven students to receive the various scholarships available, and the recommendations were approved.

A communication from the Board of Education was read recommending a graduate from the Central High School, and one from the Northeast Manual Training School for scholarships, and these recommendations were approved.

A communication was read from H. H. Cregg, of the Class of 1883, requesting a duplicate diploma, which was granted under the usual condition.

A communication was read from the Secretary of the State Board of Pharmacy relative to a Certificate of Actual Attendance at the Lectures and Laboratories of those graduates of the College who desire to take the examination for Registered Pharmacist. After considerable discussion, a committee consisting of Professors Remington, Sadtler, and Lowe, was appointed to formulate and put in effect such a method.

November 1, 1910. Twelve members present.

Committee on Library reported a decided improvement in the work and management of the Library. Library rules also the State law relative to mutilation of books and library property were displayed in the Library.

Committee on Instruction called attention to the Special Lectures arranged for 1910–1911, and urged that the attention of the students, especially the graduating class, be directed to these lectures.

Committee on Announcement reported that the October Bulletin, No. 1, Vol. 3 was ready for distribution.

Communications were read from students to whom scholarships had been awarded, expressing their appreciation.

A communication from the Board of Education was read, recommending Karl N. Krogh, a graduate of the Southern Manual Training School, as worthy of a scholarship, and on motion, this award was made.

The Treasurer reported that five thousand dollars ($5000) had been paid on account of the mortgage.

C. A. Weidemann, M.D.,
Recording Secretary.

December Pharmaceutical Meeting.

The regular Pharmaceutical Meeting of the Philadelphia College of Pharmacy was held on Tuesday afternoon, December 20, 1910, at 3 o'clock, Mr. E. M. Boring presided.

Mr. Clarence M. Kline read a paper on "The Thirty-Sixth Annual Meeting of the National Wholesale Druggists' Association held at Dallas, Texas, November, 1910," which will be published in a later issue of this Journal. The paper was discussed by Professor Kraemer, Dr. C. B. Lowe, Mr. Kline, and the chairman.

Mr. Kline submitted a copy of that portion of the General Code

of Ohio relating to paints, white lead and turpentine. Its provisions are as follows:

SEC. 6331. No person, firm or corporation shall expose for sale or sell within this state, paint, turpentine or linseed oil, which is labeled or marked so as to tend to deceive the purchaser thereof as to its nature or composition, or which is not labeled as required by this chapter.

SEC. 6331-1. No person, firm or corporation shall manufacture, mix for sale, sell, offer for sale, for other than medicinal purposes, under the name of turpentine, or spirits of turpentine, or any compounding of the word turpentine, or under any name or device illustrating or suggesting turpentine, or spirits of turpentine, any article which is not wholly distilled from rosin, turpentine gum, or scrap from pine trees, and unmixed and unadulterated with oil, benzine or any other foreign substance of any kind whatsoever, unless the package containing same shall be stenciled or marked, with letters not less than two inches high, adulterated spirits of turpentine. Nothing herein contained shall be construed as prohibiting the manufacture or sale of any such compound or imitation, providing the container shall be plainly marked, and the purchaser notified, as aforesaid.

SEC. 6332. The term "paint" as used in this chapter shall include oxide of zinc, red lead and white lead, dry or in any kind of oil, and a compound intended for like use, colors ground in oil, paste or semipaste paint, and liquid or mixed paint ready for use.

SEC. 6333. The label required by this chapter shall clearly and distinctly state the name and residence of the manufacturer of the paint, or of the distributor thereof or of the party for whom it is manufactured, and show the name or names of any substance or substances used in quantities sufficient to be dangerous or injurious to human life or health whether through absorption, contact or inhalation. The label shall be printed in English language in plain legible type in continuous list with no intervening matter of any kind.

SEC. 6334. The label on paint sold by measure shall show the net measure of the contents of the container, and on paint sold by weight, the net weight of the contents of the package.

SEC. 6335. The possession of an article or substance improperly marked or inaccurately labeled as provided in this chapter, by a person, firm or corporation dealing therein shall be prima facie evidence that it is so kept in violation of this chapter, and the penal statutes relating thereto.

SEC. 6336. The dairy and food commissioner of Ohio shall enforce the provisions of this chapter and the penal statutes relating thereto, and such commissioner, his assistants, experts, chemists and agents shall have access and ingress to the places of business, stores and buildings used for the sale of paint, turpentine or linseed oil, and may open any package, can, jar, tub or other receptacle containing an article that may be sold or exposed for sale in violation of such provisions or statutes. The inspectors, assistants

or chemists appointed by such commissioner, shall perform like duties and have like authority under this chapter and the penal statutes relating thereto as is provided by law in other cases. Such commissioner shall publish bulletins from time to time giving the results of inspections and analyses, with such other information as he deems suitable.

SEC. 13168. Whoever violates any provision of the law relating to the labeling of paints, mixed paints and similar compounds or white lead by manufacturers or distributors thereof, shall be fined not more than fifty dollars, and for each subsequent offense, shall be fined not less than fifty dollars nor more than one hundred dollars, or imprisonment not less than thirty days, nor more than one hundred days, or both.

Professor Remington presented, on behalf of E. M. Roche, a pharmaceutical recipe book.

Professor Kraemer exhibited the "Tabloid" Photographic Outfit no. 906," put up by Burroughs Wellcome & Co. This comprises a compact equipment of "Tabloid" photographic chemicals for developing and fixing plates, films, papers, and lantern slides; and also "Tabloid" chemicals for intensifying, reducing, sepia toning, copper toning, hardening, clearing, restraining, etc. Sufficient chemicals are provided to make several gallons of solutions in large or small quantities, fresh and vigorous for each occasion, without the trouble of weighing and without waste. A copy of the Wellcome Photographic Exposure Record and Diary, a complete pocket guide to success in field and dark room, is also included. The whole is packed so as to be convenient in travelling.

Professor Kraemer stated that he had found the Wellcome Photographic Exposure Record and Diary a convenient book for recording field work in photography and the Wellcome Exposure Calculator very useful in determining the time exposure to be given.

On account of the difficulty in making good photographs, due to the difficulty in estimating the proper exposure, this book with its simple instructions should prove of great service to the photographer, no matter where or under what condition exposures are made. Again as it is frequently desirable to develop the plates before returning home, this compact equipment of photographic chemicals supplies a want which will be appreciated by photographers who are making exposures away from home.

A complete collection of ground emery samples, received from Walter C. Gold, of Philadelphia, were presented on his behalf by

Professor Kraemer, who also called attention to a specimen of the "Jungle Plant," *Combretum sundaicum,* which he had received from a fellow member, Henry C. Blair.

George C. Goess, of Philadelphia, presented a bottle of Church's Cough Drops which sample is said to be 120 years old. Professor Kraemer remarked that it might be of considerable interest in the years to come if the College had a collection of Proprietary Medicine, many of which in a few years would probably be no longer obtainable, and that the interest in them would lie chiefly in their illustrating a method of medication in vogue at a particular period.

Mr. Henry C. Blair presented an excellent specimen of bauxite from Georgia and a unique specimen of wood carving representing the seven idols of China, each idol being from 3 to 5 cm. long.

President French presented a collection of silver ores which he obtained during a recent trip to Colorado.

Mr. E. H. Eppler, of Philadelphia, presented a hand balance which was used by Professor Maisch in his old store at 1610 Ridge Ave., Philadelphia.

A vote of thanks was tendered the donors for the various articles presented to the College as also to Mr. Kline for his communication.

H. K.

CORRESPONDENCE.

U.S.P. & N.F. Compulsory in New York State .

To The Editor of The American Journal of Pharmacy.

Sir: Attention is called to the change of rules by the New State Board of Pharmacy and approved by the regents that every pharmacist and druggist in the State of New York must possess a copy of the latest edition of the U.S.P. and N.F.

The rule of the old Board required a copy of the U.S.P. or some other publication embodying its text in full. Rule 7 of the New State Board of Pharmacy reads as follows:

"Every pharmacy and drug store shall own and have on file at all times the eighth decennial revision of the Pharmacopœia and the

latest edition of the National Formulary and no registration certificate shall be issued till it complies with this rule."

It is of course also advisable to have a dispensatory as a reference book in well regulated pharmacy. As the rule is very likely to be enforced I earnestly advise your subscribers in New York State to supply themselves with copies of the N.S.P.VIII and N.F.III which books can be obtained readily through the wholesale drug trade.

Let us hope that other State Boards of Pharmacy will follow this example, in fact that State Laws will be enacted and enforced making the possession of a copy of the latest edition of the U.S.P. and N.F. compulsory in every pharmacy and drug store in the U.S.

OTTO RAUBENHEIMER, Ph. G.

THE AMERICAN
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THE BIOLOGICAL STANDARDIZATION OF DRUGS.

By Worth Hale, M.D.,
Assistant Pharmacologist, Hygienic Laboratory, U.S.P.H. and M.H. Service, Washington, D. C.

Pharmacy calls for accuracy as applied to remedial agents. Absolute and unfailing accuracy to the limits of scientific knowledge and unvarying honesty are fundamental principles to be emphasized and dwelt upon from the beginning of a course in Pharmacy or of medicine, until the last prescription is compounded. There should be no guess work and every effort on the part of pharmacist or doctor or laboratory worker to promote greater exactitude so far as drugs and medicines are concerned is to advance the healing art. Nor is it an unworthy ideal for carelessness in the field of drugs and medicine is scarcely less dangerous than for railroad engineers to guess at the color of signals and there is no questioning that hundreds of people are annually killed because such haphazard and commercial methods have been used in preparing drugs that they do not have the virtues expected of them.

We too often forget that not only medicine but also pharmacy is a business dealing in life and health. It is trite to say that human life often hangs upon a thread and that the merest incident may determine the issue; that the failure of a drug to have the strength it is supposed to have because of impurity or dangerous deterioration or adulteration or lack of active principles

means delayed convalescence or even death. (1) These are statements which may sound a trifle theatrical. One can not often prove them. If a patient is made more violently ill or dies no one suspects that the medicine was at fault. It is a visitation of providence or, as the facetious would have it, a doctor was called and then the undertaker.

My attention has recently been called to a case of poisoning. The patient, who suffered from chronic heart disease, had been receiving tincture of strophanthus in a certain dose. The prescription was refilled and the medication continued. After the second dose from the new strophanthus tincture poisonous symptoms developed although fortunately ultimate recovery ensued after two days of serious illness. An assay made at this laboratory of the strophanthus showed that it was an exceedingly active preparation and whereas the patient was supposed to be receiving the same dose as of the old he actually received an amount of the active principle in this new preparation equal to about three times that of the strophanthus tincture which he had formerly been taking.

In the opposite direction I have a report on a digitalis preparation which upon examination proved to be distinctly depressing to the heart and not a tonic. Who would dare say that the administration of this drug to an already overburdened heart would not produce the most disastrous results. A physician in Baltimore made inquiry of the firm exploiting this preparation. The firm replied that we had made an effort to secure an old and deteriorated sample for our examination. Like certain other extravagant claims made by an occasional manufacturer this statement was a bald untruth to save their own reputation and was absolutely without foundation. The facts are that the original bottle was ordered by our pharmacist from a local jobber and the jobber had no information whatever that the drug was to be tested. It was just such a bottle as would have been dispensed on a physician's prescription.

Upon facts such as these, and the number of specific instances could be multiplied almost indefinitely, the whole theory of drug standardization rests. Any consideration of quality from a commercial standpoint is wholly secondary and drugs should be standardized or assayed that the patient may receive of potent remedies always and invariably the amount of active substance prescribed: and when this has been done the pharmacist has given the best

of his skill as an aid to that of the physician to the cure of the sick.

The committee in charge of the revision of the recent editions of the pharmacopœia have clearly recognized the need for suitable standards especially for the more potent drugs in order to eliminate the danger and inaccuracy in the administration of remedial agents. Thus in the sixth and seventh and eight revisions of the Pharmacopœia we find tests and assay processes introduced while in the Eighth revision a further notable advance was made, in the adoption of a standard for diphtheria antitoxic serum. There are a number of very important drugs long used in medicine and more recently also certain biological products for which chemical tests or assay methods are not available owing to the fact that the chemistry of these substances either is not known or they are of such a character that quantitative methods can not be successfully employed. For these, biological tests and standards have been proposed although excepting that for diphtheria antitoxic serum none have as yet been officially adopted. The recent Pharmacopœial convention however adopted a general principle reading as follows:

"It is recommended that biological tests or assays, when accurate and reliable, may be admitted."

In the group of drugs for which chemical standards are not at the present time available are digitalis, strophanthus, convallaria, squills, apocynum, preparations of the suprarenal glands, ergot, and cannabis indica.

It is somewhat surprising in view of the great importance of some of these drugs that, although biological tests were proposed nearly 50 years ago, no practical application was made until 1898. I am informed that Professor Cushny first suggested such standardization especially for the digitalis group but the first paper relating definitely to the subject was one in October, 1898, by Houghton who worked in Cushny's laboratory. Since Houghton's paper the subject of Biological Standardization has attracted a good deal of attention from pharmacologists and more recently also from progressive drug manufacturers and pharmacists.

The drug, or rather group of drugs, upon which the most work has been done is the digitalis group, it being generally conceded that a method applicable to one member as digitalis itself would be applicable equally to strophanthus or squills. As a result

no less than 15 or 20 methods have been proposed for their assay. So much discussion of these methods has been indulged in and so many statements more or less supported and often unsupported by experimental evidence have been offered by the exponents of a particular method that it seems worth while to take up the various phases of the problem at this time, and this especially because of the possible, and I hope probable, adoption of some method by the committee of revision of the next Pharmacopœia.

If accurate and reliable are the modifying phrases in the recommendation of the Pharmacopœial Convention regarding biological standards. How accurate; How reliable—Digitalis preparations, tinctures, fluidextracts, tablet triturates, and hypodermic tablets, as purchased direct from the manufacturers, vary about 400 per cent. in activity. Is the revision committee willing to adopt any method which will reduce this enormous variation to 50 per cent? I am absolutely certain it will mean that lives will be saved every year. If any biological method will reduce the variation of the preparations on the market to 25 per cent. instead of 400 will it be worth while? Will it be accurate enough? I would much prefer that I myself should be assured by the Pharmacopœia of a drug with no more than 25 per cent. variation rather than to take my chances with a drug now of one strength and on a refilled prescription one or four times the strength.

In this country four methods have been proposed, namely, Houghton's twelve hour frog method, Reed and Vanderkleed's method using the guinea pig, a method proposed by Hatcher using the cat; all of these methods depending on the determination of the least fatal dose for the animal in question, and finally the method proposed by Famulener and Lyons, that of determining the least amount of the drug to stop the heart of a frog in one hour.

Houghton's method is to choose frogs of about the same weight and inject them with a given amount of the drug. If, at the end of 12 hours, the animal is dead the dose is reduced, if alive the dose is increased. By use of a series of frogs with varying doses the assay may be hastened. An experiment published in the AMERICAN JOURNAL OF PHARMACY indicates that 3 days were required to make the assay, and the assay required the use of 14 frogs, the cost of which in any section of the United States including express charges would be under one dollar. In Washing-

ton the cost would be 60 cents for frogs shipped 800 to 1000 miles.

Reed and Vanderkleed's method of assay is probably well known to you. I quote from a recent article by Githens and Vanderkleed. "Guinea pigs are first weighed and then to one pig is given hypodermically the standard minimal fatal dose as determined by a large series of experiments on guinea pigs, to a second 9/10 of this, and to a third 11/10. If the drug is of the proper strength the two pigs receiving the larger dose will die, the third will recover. If two pigs live the dose is increased by tenths until two die. If all three die the dose is reduced by tenths until a pig lives." The cost of animals at Washington would be not less than $2.00 and the assay would take, I presume, about a day. However, in testing out this method for myself the smallest number of animals used in an assay was 7, the largest number 18, the average of the test of 8 different preparations being 11 which would cost us $5.50 per assay and the time required would be extended to at least two days. Further, certain animals survived doses 20 per cent. larger than had killed others. Thus, 4 were killed with 0.5 mgm. per gram body weight, 3 lived with 0.6 mgm. doses of the same drug.

Hatcher's method is the most complex of all although he suggests that the retail pharmacist would find it available for his use on account of its simplicity. That certainly will make it appear attractive even though it is undoubedly the most difficult of all the American methods.

In this method a cat is anæsthetized, the femoral vein is exposed and a cannula introduced. Then into this the digitalis preparation is slowly injected and the injection stopped or continued slowly when toxic symptoms such as irregularity of the heart and respiration, convulsions, etc. are seen; the end reaction is the death of the animal.

A modification of this method is to inject about 75 per cent. of the supposed fatal dose which is followed by the injection of ouabain which acts like digitalis but more rapidly until toxic symptoms appear, the drug is then continued more slowly until death results. For this method an accuracy of within 3 per cent. has been claimed, but from later investigations Hatcher says a number of cats have been found which tolerate doses nearly 50 per cent. more

than in his earlier experiments. In inexperienced hands the variation would probably be even greater.

These methods all depend on the estimation of the least fatal dose, but for reasons to be given such an end reaction appears to me to be undesirable. Digitalis glucosides act not only on the heart but also directly on the central nervous system first stimulating and then depressing it. In these general toxic methods the drug is given in sufficient doses to cause death without reference to the organs chiefly affected and no one can say, although much theorizing has been indulged in, whether the death is the result of an action on the heart or on the brain or, and I think it extremely likely, a resultant of the action on both brain and heart.

The method is usually carried out using mammals and while this is believed by some to be a step in the right direction on account of the closer relation between the higher animals when compared to cold-blooded animals (frogs) and man certain experimental evidence tends to show that this is not necessarily so. At least it is to be noted that death in such animals in certain cases apparently resulted from a paralysing action on the central nervous system while the heart as recorded by blood pressure tracings was still in good condition. In other cases the respiratory movements were kept up some time after the heart had stopped beating and the blood pressure had fallen to zero. Further the allegation that these effects on the central nervous system are all secondary to the heart action is contrary to the known facts of Physiology.

In this connection it is further urged that a digitalis preparation with a high percentage of the saponin like body, digitonin, would easily cause death from the action of this poison which depresses both the heart and the central nervous system. Thus such a preparation would probably show a high value by a general toxic method although the heart tonic principles might be present in relatively small amounts, or of two preparations with the same proportion of substances acting on the heart that with the larger amount of the saponin like body would assay stronger. In the general toxic method in which frogs are used, as in Houghton's "twelve hour method," this objection would naturally lose some weight on account of the ability of such animals to live a considerable time independently of the central nervous system, the action of the drug being therefore presumably upon the heart.

As a further objection it may be suggested also that a general toxic method would not show adulteration or accidental contamination of a digitalis preparation since a lethal effect could easily be secured from an action of any of a number of poisons or possibly also from substances formed in the deterioration which digitalis preparations are known to undergo. To be certain of a heart tonic, a digitalis action, such a method would need to be controlled by tests upon the heart itself.

The other type methods are based on a general principle which it would seem worth while emphasizing—namely, *that any biological assay method for any drug should take into account that action of the drug upon which its chief therapeutic usefulness rests and that in so far as practical difficulties did not interfere this action should be made the basis of the biological method used in its assay.* In the case of the digitalis group it would seem of considerable importance, if this be true, that the end reaction should be one involving the characteristic effect of the group upon the circulation apparatus and this can be done on mammals only by making use of recording devices and maintaining artificial respiration.

The type method of determining the comparative value by noting their effects upon the heart, especially of the frog, is perhaps the oldest and at the present time the most widely used of all methods as it is used by at least three manufacturers in this country and exclusively in Germany.

Three sub-methods may be described although others are occasionally used; in one the drug is given to the intact animal which is subsequently operated on to note the condition of the heart, in another the drug is given to the animal subsequent to the operative procedure in which the heart is exposed. In the third the heart is removed from the body and perfused; however, the last named methods are not used in this country and will not be discussed on that account in this paper.

The first sub-method, that of examining the heart at some time subsequent to the injection of the drug, the chief points of differences in the manner of experimentation has been in the time at the end of which the heart of the frog should be found in complete systole. Time limits varying from thirty minutes to two hours have been used.

This method has been provisionally adopted at this Laboratory for testing digitalis and allied preparations. The general method

of procedure is essentially the same as that suggested by Famulener and Lyons[1] in which permanent systole of the frog's ventricle at the end of exactly one hour is taken as the end reaction. Some slight modifications have been made, the chief of which is that the assays are all carried out at a constant temperature as it is believed that this precaution results in greater accuracy. The drug is injected through the mouth into the anterior lymph sac of the intact frog (Rana pipiens) and at the end of an hour the animal is pithed (both brain and cord) and the thorax opened. The condition of the heart is then noted and a smaller or larger dose is injected as indicated. To hasten the assay a series of three frogs is usually given doses which vary quite widely and an approximate dose is estimated from these preliminary results. By successively narrowing the limits of dosage that amount just necessary to produce the end reaction may be determined by the use of from 8 to 12 frogs.

The method has the advantage of comparative simplicity so far as operative technique is concerned. The animals are always easily obtained which is a very important consideration and if the storage tanks be kept at a suitable temperature (10° to 15° centigrade) they remain active and healthy for months. In this connection it is worth while calling attention to the difficulty of obtaining a suitable number of mammals, especially cats, rabbits, or dogs, for carrying out such tests on warm blooded animals when a large number of assays are to be made. Of less importance also is that of cost. Frogs for each assay will cost approximately fifty cents. If mammals are used, on the basis that at least three to five should be used for each assay, the cost would be from two to three dollars while to this would be added the expense of food supplies, etc., which in the case of the higher animals is a considerable item.

While thus expressing my belief in the frog as a suitable and, despite certain elemental precautions, a convenient animal for assay purposes it has never been shown to what degree biological assays, using either frogs or other animals, were accurate and especially as showing the therapeutic potency of a given preparation.

Unknowns made up by a chemist in the Division of Pharmacology were assayed and the results of these assays are grouped

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[1] Famulener and Lyons: Proc. Am. Pharm. Ass., 1902, **50**, 415.

together in the following table not only as a means of comparing the activities of the various so-called pure principles but also to show, in tabular form, the amount of error which is to be expected when using a frog-heart method of assay.

Drug	Assay Value [2] 1910	1902 [3]	Unknown Solutions per cent. error. 1	2	3	4
Strophanthin	0.000,001,10	0.000,000,5	1.8	2.9	3.1	1.4
Convallamarin	0.000,004,75	0.000,004,5	8.6	10.6	7.4	9.0
Digitoxin	0.000,008,50	0.000,008,5	7.2	3.8	0.7	5.2
French Digitalin	0.000,013,00	0.000,015	1.6	3.8	3.6	2.6
Digitalein	0.000,024,00	0.000,032,5	4.5	3.8	6.0	1.5
German Digitalin	0.000,070,00	0.000,022,5	2.5	2.8	5.9	0.0

From this summary it is apparent that strophanthin is the most active, the German digitalin (Digitalin purum Grübler) is the weakest and that digitoxin the most active of the digitalis glucosides, is about 8 times less active than amorphous strophanthin. It is not urged on the basis of these experiments, however, that in the clinical use of these substances doses be given proportionate to these values. But in so far as secondary factors, such as rate of absorption and elimination, do not interfere proportionate doses would probably give like therapeutic results. Elemental tissues such as the heart muscle, no matter from what animal species, react qualitatively the same. As pointed out by Cushny [4] the action of the digitalis group upon the frog's heart is strictly analogous to the action on the mammalian heart with differences in action, dependent upon a stronger vagus activity in the higher animal species. In the therapeutic use of the drug only the first stage which consists of a minimal activity of the vagi and a definitely increased activity of the muscle substance itself is desired. The action on the frog is almost purely a muscle action and it is upon such grounds that biological assay methods on the lower forms of animal life are believed to give results which are capable of direct utilization in therapeutics.

On theoretical grounds, therefore, there is no reason why assays using frogs will not give results which may not be depended

[2] Amount in gram per gram body weight of Rana pipiens to cause permanent systole of the ventricle in one hour.

[3] Famulener and Lyons.

[4] Cushny: Pharmacology and Therapeutics, 1906, p. 466.

on by the clinician and which may be used as a basis for dosage as safely as if assays were carried out on guinea-pigs, rabbits, cats, or dogs and so far as the evidences of accuracy and totality of action go far more safely than if carried out by estimating the single active constituent digitoxin or digitalin by chemical means. Assays, as is to be noted by the above summary, may be made using frogs (possibly also other animals) which will give an estimate of the amount of glucosides in a solution to within a few (1 to 10) per cent. of absolute accuracy.

In all cases in therapeutics the unknown factors of absorption, elimination, and susceptibility will persist in spite of all attempts at assaying the preparations of the digitalis group. But these factors would also exist in like degree as long as several differently active bodies and resinous substances are to be reckoned with even if absolute chemical assays of not one but all the active glucosides of the group were possible. The frog method of assay gives all any assay method can possibly give, that is, a definite index of the amount of active substances, and what is especially important an index of the activity of *all substances* in the preparation which act upon the heart.

Certain factors regarding variation in reaction of frogs to the digitalis group of glucosides, or to other poisons, are of little importance aside from increasing to a very slight degree the complexity of the assay process. The whole question resolves itself into a matter of using a digitalis preparation of known activity and keeping quality (and for this purpose crystallized digitoxin or ouabain is suggested) to standardize the frogs at the same time that the unknown is assayed. In this way accurate results may be obtained without reference to season, age, sex, temperature conditions, or species of frogs used.

I have purposely discussed at some length the frog-heart method as proposed by Famulener and Lyons and it may be regarded somewhat as a personal matter with me since I use it that I should give it so much time. I have tried not to make it so and have approved of it because in my best judgment it was based on perfectly sound physiological facts as well as experimental evidence for, excepting Hatcher's cat method, all these methods have been reviewed after personal investigation and the whole matter considered as impartially as possible previous to its adoption. It is a fact, however, that long acquaintance with a particular method

is apt to lend some bias to one's judgment and also because of longer experience one naturally obtains more uniform with the method he is accustomed to use.

I wish to go on record, however, as believing that the adoption of any one of these methods will give to those who need digitalis medication a vastly more uniform drug than is now obtainable. Absolute accuracy cannot be expected, but there can be no question that a comparatively accurate assay of digitalis is possible with variations not exceeding 10 per cent. in the therapeutic activity of the drug.

Ergot:

Ergot, the drug next in importance to the digitalis group, is used especially at child birth to promote contraction of the uterus and to thus prevent dangerous and even fatal hemorrhage. At the present time there is no known way to assay ergot accurately by chemical means, but it is known from clinical as well as physiological tests that many samples of ergot on the market are absolutely devoid of a typical ergot action, thus often exposing mothers to one of the most feared accidents of child bearing.

The chemistry of ergot is becoming better known and at the present time some five active constituents have been pretty certainly isolated in a pure state. These are ergotoxine and ergotinine, which are characteristic of ergot, parahydroxyphenylethylamine, betaimidoazolylethylamine, and guanidobutylamine—the amines being found also in other places as in the decomposition of meats. Of these, ergotoxine causes a marked contraction of the pregnant uterus and also a certain amount of contraction of the non-pregnant organ. In addition it also causes bluing and gangrene of the cock's comb and causes an increase of blood pressure. Ergotinine has little or no activity but is closely related chemically to ergotoxine. One of the amines causes a rise in blood pressure, another a fall, but both cause contraction of the non-pregnant uterus. It has by no means been clearly established what their effect is upon the pregnant organ. The third amine has not been tested physiologically. In addition there is no reason to believe that there may not yet be some half dozen other bodies all with more or less action on the uterus.

For digitalis chemical methods may at some time be available, but it seems absolutely unlikely that a chemical assay will ever

show the therapeutic activity of ergot. Biological tests, however, have been used for many years and to Kobert and Grunfeld may be given the honor of suggesting a method of biologically determining the activity of this drug. The method is that of producing the characteristic bluing or gangrene of the cock's comb and in 1898 Houghton applied such a method commercially. In this method the drug is fed or injected intramuscularly into roosters, in such a dose as to cause bluing of the comb and I believe in all cases comparing the intensity of this action with some standard preparation.

A second method is that of estimating the amount of rise in blood pressure as a result of a given dose. The stronger the preparation, the higher the blood pressure in direct proportion. A third method is that of using the uterus itself as a test object, some workers carrying on the experiments on the intact animal and others on the organ isolated from the body. Usually cats are used, but dogs, guinea pigs, and rabbits have been tried, with less satisfactory results, however. The drug to be tested must be compared with a standard preparation carrying out the test upon the same organ since different uteri react very differently.

Recently also Dr. Wood has suggested a chemical method based on the estimation of the benzole extractive, probably an impure ergotoxin, after precipitating the ergot with water. The increase in the amount of extractive was found by him to increase proportionally as the increase in blood pressure on injection of the drug in dogs. His premise is that blood pressure estimations are a true index of the activity of a given preparation and hence concludes that the benzole extractive is an accurate index of the drugs therapeutic properties.

A further chemical method is the estimation of the Cornutine content of ergot—cornutine being an impure mixture of ergotixine and ergotinine.

Dr. Edmunds of the University of Michigan and I have been engaged in a study of the assay processes for this drug. This investigation is not yet quite completed but both of us feel that certain facts are fairly well established.

The chemical methods of Dr. Wood and Professor Keller were used. In all cases duplicate and in certain instances quadruple estimations were made of both the cornutine content and the benzole extractive. Rippetoe's modification of Wood's method,

that of taking an aliquot part, was also tested and gave results corresponding closely.

The three biological methods were also employed. Cocks of the Leghorn variety and of nearly pure blood were chosen for observations on the cock's comb. Mongrel roosters cannot be successfully used on account of individual variation. We have also some evidence that they should be of the same age, the older roosters apparently being more resistant. The drug was injected into the breast muscle as a rule but in a few instances into the thigh. The doses ranged from 1 to 4 c.c. of the fluid extract and in each instance a control rooster was injected with one of the preparations which we used as a standard. A minimal bluing was regarded by us as the best for making the comparisons but doses above and below this were given to insure greater accuracy of results. In this way differences of probably 15 per cent. could be determined.

In the blood pressure work dogs anæsthetized with morphine were used and the drug in the dosage recommended by Wood was injected into the saphenous vein. The average of the maximum rise, the 5 minute and the 10 minute rise in blood pressure were taken as the index of the drugs activity.

In the uterus method cats were employed for all determinative readings. For the intact animal, after anæsthesia, using chloral and ethyl carbamate, the animal was submerged in a large tank filled with salt solution to protect the uterus from the air. The abdomen was opened and a lever attached to the uterus. The drug was injected through a cannula into a vein. A standard drug as a basis of comparison was injected alternately with the ergot preparation under consideration and the effect on the uterus recorded by the lever on a smoked paper.

The work on the isolated uterus is much simpler. The animal is either killed outright or anæsthetized and the uterus removed. Only a very short section of this organ is used—in the contracted state not over a centimetre in length; this is put in a small constant temperature bath which is filled with an oxygenated physiological salt solution after the formula of Locke. The organ is then attached to a writing lever in order to secure a record of its movements.

Uterus tracings from different animals differ widely in character which makes the effect of ergot difficult to read. After some

experience, however, and after securing a large number of readings, all of which may be made on the same organ, a fairly definite idea may be obtained of the strength of the drugs, the standard and the unknown.

As a result of these studies we have arrived at certain conclusions basing them on the comparative values obtained from assays of a number of commercial preparations using the five methods outlined above.

The three biological methods showed a very fair agreement while the results from the uterus and cock's comb methods showed an extraordinary one. This was a matter of considerable surprise to us since we had believed from a rather limited experience that the cock's comb method would not give concordant results. In this series there appeared to be an almost exact parallelism between these two methods throughout the series. The blood pressure method was generally concordant but in certain instances showed a wide variation from the results by the other methods.

The two chemical methods did not show any definite relation to the biological methods although there was some agreement. The cornutine of Keller more closely paralleled the biological tests than did the benzole extractive of Wood, only three of the latter estimations in 11 experiments corresponding to the rise in blood pressure.

Just how closely the therapeutic value of ergot corresponds to the activity as expressed by these assays cannot be definitely determined because of the complexity of the chemical substances found in this drug and also because of the variability in their actions. There is sufficient evidence to show, even if the relation is not an exact one, that there is a fairly close correspondence, however, as is evidenced by the surprising agreement between the results by various biological methods. I am also convinced as with digitalis that the adoption of any one of these methods will result in the production of infinitely more uniform preparations of ergot than can now be obtained. The limits of variation from a given standard, as a definite amount of ergotoxine, would probably need to be fairly wide, but even with a standard allowing of considerable variation a great deal would be gained for obstetrical patients who, as matters now stand, often gain nothing from the administration of this important drug because of its inactivity.

I stated in the beginning as an ideal that we should aim for

absolutely accuracy in all matters relating to drugs and this can only be secured through official recognition of some standard and a method of assay. Where accuracy of assay cannot be absolute it certainly is no unworthy ideal to ask in behalf of the sick for relative accuracy and uniformity such as biological assays and standards will give and I hope that it is not too visionary to think that biological methods at least for the digitalis group, for ergot and for suprarenal gland preparations may be adopted by the Pharmacopœial revision committee.

SURGEONS GRIT SOAP.

By John K. Thum, Ph.G.
Pharmacist at the German Hospital, Philadelphia.

The thorough cleansing of the surgeon's hands previous to a surgical operation is of the utmost importance. Vigorous rubbing with soap and hot water, and plenty of it, is the usual initial performance in sterilizing the hands of the operator.

Lately, in place of the ordinary hard, soft, or liquid soap, some surgeons are using a grit or pumice soap. For reasons that are obvious, all dirt and foreign matter adhering to the hands are more easily and readily removed.

For some reason the manufacturers of these pumice soaps make them exceedingly alkaline. As can be easily imagined this excess of free alkali is very prone to destroy the epidermis and render the hands of the surgeon sore and unsightly. For this reason the surgeon at the institution with which I am connected has ceased to use the commercial pumice soap and instead is using one of our own manufacture.

This soap was made by boiling cottonseed oil with strong solution of sodium hydroxide for one-half hour, adding a small quantity of alcohol to facilitate saponification, and precipitating the soap with a 20 per cent. solution of common salt. Common salt not only separates the soap but it also rids it of nearly all free alkali. The mixture was then thrown on a strainer and allowed to drain. The precipitated soap was then washed with distilled water and expressed. Powdered pumice was next added and thoroughly incorporated. The soap was then put into a suitable mold and placed, well covered with gauze, in a cool dry room, to harden.

This method had its disadvantages, however. It required from five to six weeks to become firm and hard enough for its intended use. It also was somewhat brittle. This, however, was overcome to some extent by using potassium hydroxide instead of the sodium hydroxide, but the length of time for hardening was not materially decreased. Of course, this could have been overcome by using animal fat or tallow, but it is not always practicable or possible to obtain this readily.

It then occurred to the writer that stearic acid and cottonseed oil in equal proportions might produce a soap that would harden at once or in much less time than the method described above.

Accordingly some experimentation was carried on with this fatty acid and cottonseed oil and the results were both encouraging and satisfactory. So much so in fact, that the following formula and method of procedure was finally decided upon as yielding the better product.

Cottonseed oil	500 c.c.
Stearic acid	500 Gms.
Sodium hydroxide	150 Gms.
Alcohol	150 c.c.
20 per cent. solution sodium chloride q.s.	
Distilled water q.s.	
Powdered pumice	300 Gms.

Heat the cottonseed oil and stearic acid until the acid is completely dissolved. Then add the sodium hydroxide, dissolved in a litre of distilled water, and heat for 15 minutes with constant stirring. Next add the alcohol and stir until saponification is effected. This is noticed by the mixture becoming homogeneous in a few minutes. Then add one litre of a 20 per cent. solution of sodium chloride and stir vigorously. Allow to stand until the soap is hardened; the alkaline liquid, which remains at the bottom of the container, is then drained out by punching a hole in the soapy mass on one side. It is then washed two or three times with distilled water, melted, and while still on the fire, the powdered pumice is added, and the whole thoroughly incorporated. While still hot it is poured into suitable moulds. In twenty-four hours the soap is sufficiently hard enough for use.

A STANDARD FOR TINCTURE OF CARAMEL.*

By Geo. A. Menge.

The subcommittee in charge of color standards to be incorporated in the new National Formulary has under consideration two methods for the color standardization of tincture of caramel; by comparing it, or a given dilution with water, with a solution having a readily reproduced color value. The first of the methods proposed provides for a comparatively dilute solution, prepared as follows:

"Place 0.5 Gm. sugar in dry test tube 20 mm. diameter. Immerse the tube to a depth of 5 cm. in a sulphuric acid bath, previously heated to 210° C. and keep at that temperature for 20 minutes. Remove the tube and when cold dissolve in sufficient water to make 200 c.c. Add 50 c.c. alcohol and sufficient water to make *exactly* 250 c.c."

A modification of this method has been suggested by Mr. Raubenheimer to the extent of substituting a bath of petrolatum at 200° C. for the sulphuric acid at 210° C.

The second method now in the hands of the subcommittee as modified by Mr. Raubenheimer, reads as follows:

"On a sand bath heat 100 gm. of sugar to 200° C. and keep at that temperature for one hour, stirring constantly—then add sufficient water to make 100 c.c. when cold."

From the point of view of the pharmacist the first method seems to me to be practically impossible. It obviously could not, with reason or common-sense, be applied without the advantage in equipment of a very effective *enclosed* hood—and such an advantage, I take it, is not common. To apply it without such equipment would entail great discomfort, if not more serious consequences. The fumes of sulphuric acid at 210° C. are abundant and more or less destructive, and their effect upon fixtures, upon pharmacists, and

* Read at the meeting of the City of Washington Branch, Am. Pharm Ass'n., held February 11, 1911.

upon any customers that might be at hand may reasonably be described as intolerable if, by any possibility, avoidable.

Furthermore, the size of the vessel and the volume of acid required for the application of this method is quite considerable—sooner or later a beaker or other container would break, and sulphuric acid at 210° C., splashing around on fixtures and operator is another unpleasant possibility, associated with this method.

The suggested substitution of petrolatum for sulphuric acid seems to me to only change the character of danger and discomfort without greatly reducing either.

The second method, while doubtless safe, would seem to be barely less objectionable in the detail of fuming. To heat *100 Gm.* of sugar to *200° C.* for *1 hour* would surely caramelize the whole store—certainly the man who had to stand and stir for *one hour* would become thoroughly saturated with the odor of burnt sugar. Moreover the big time factor involved makes the method objectionable.

In attempting to devise a more practical method than the two described above, I have conducted a series of experiments to determine quantitatively the effect of sulphuric acid in direct contact with sugar as a means of producing colored solutions of the desired tint.

Without taking time to describe experiments it is perhaps sufficient to say that I finally succeeded in obtaining a solution which conformed exactly, or very nearly so, to the color produced by the first method.

The proceedure is as follows:

Make a sulphuric acid solution by adding 2 c.c. of pure concentrated sulphuric acid (specific gravity 1.84) to 12 c.c. of water. Take 0.5 Gm. of sugar in a test-tube—add 5 c.c. of the acid solution described above, and heat the mixture in a boiling water bath, with mixture continually submerged and with constant agitation, for exactly 5 minutes. Immediately add a little cold water and then 35 c.c. of the U.S.P. test-solution of potassium hydroxide; finally dilute to 100 c.c.

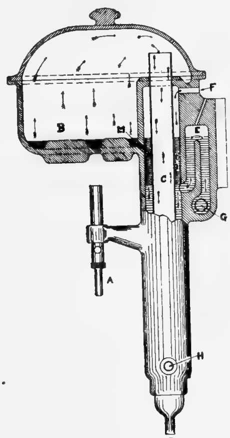
The whole procedure takes 15 minutes, is absolutely without danger or discomfort, and gives correlating results that very closely approximate those obtained by the first method outlined.

AUTOMATIC WATER STILL.

By F. J. Stokes.

Several papers have been published in the American Journal of Pharmacy on desirable forms of stills for pharmaceutical purposes.

Professor Procter described a still for apothecaries in the American Journal of Pharmacy for January, 1864, p. 12. This still was a modification of the apparatus described by him in 1848 in the American edition of Mohr and Redwood's Pharmacy. In the same issue (page 22) Mr. Wiegand described a still which was primarily used to recover alcohol from various preparations.



Somewhat later Neynaber (Amer. Jour. Pharm., 1865, p. 166) described an automatic pharmaceutical still in which a continuous distillation was affected. Pharmacists, generally, are familiar with the distillatory apparatus devised by Professor Remington (see this Journal, 1878, p. 15; 1879, p. 225).

Without entering into a description of the various forms of stills which have already been devised, I shall consider a new and inexpensive automatic water still which is of interest to every druggist as it produces distilled water at the remarkably low cost of one cent per gallon per hour. It is gas heated and being automatic requires no attention. It is fastened to the wall and gas and water connections can be made with rubber tubing.

The main body and condenser of the still are cast in one piece which eliminates joints and makes it substantial. The dome or cover is porcelain lined to prevent corrosion while the condenser is block tin lined. The still is supported by a wall bracket from which it can be separated or slipped, without unscrewing, for the purpose of cleaning.

The still consumes ten (10) cubic feet of gas for each gallon of water distilled or at a cost of one cent per gallon.

By a patented construction the Stokes Automatic Still accomplishes two novel results. It utilizes the steam generated for heating the feed water to the boiling point, so that a minimum of heat is required to operate it, and by this preliminary heating of the feed water the ammonia and other gases are largely eliminated.

The following is a brief description of the still and its manner of action: The feed water enters at (H) in diagram, surrounding the condenser tube (C) and serves first to condense the steam generated in the still (B). As the steam descends the condenser tube it becomes heated to the boiling point by the time it reaches the top, where the ammonia and other gases escape into the air through the passage (F). A part of the feed water flows over the goose neck (E) into the sink and the balance passes into the still through the passage (M). The still is heated by a Bunsen burner. The distilled water comes out at (J) and can be piped to any receptacle. The condenser tube extends to the extreme top of the steam chamber and high above the water level, so there is no danger of water being carried over by the steam.

THIRTY-SIXTH ANNUAL MEETING OF THE NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION.

By C. Mahlon Kline.

The Thirty-Sixth Annual Meeting of the National Wholesale Druggists' Association was held at Dallas, Texas, and while the attendance naturally was less than if the meeting had been held at a more central location, the majority of those who have been active in the Association work in the past found time to attend.

The meeting was characterized by the greatest harmony and

good feeling. Old ties of friendship were renewed, and had it not been for the discomforts afforded by the Southland Hotel, the meeting would have been in every way a memorable one. This hotel evidently calculated that the National Wholesale Druggists' Association would not be likely to meet again in Dallas for at least twenty years, and, therefore, proceeded in a cold-blooded way to make what it could out of its guests before they should escape from its clutches. One man upon being shown his room at the Hotel Southland, and finding it uninhabitable, decided to leave and go to another hotel. The management charged him for the day before and the day on which he rejected the room, before they would release his baggage. Such treatment is not calculated to make Dallas attractive as a convention city, though in the past a number of conventions have held their meetings there.

It is very difficult to separate from Texas the idea of a boundless plain, unbroken by habitation, through which wild steers gallop unrestrained. As a matter of fact a wild steer could not gallop more than a few hundred yards before coming into contact with a modern up-to-date wire fence. The state is completely fenced from one end to the other, and is dotted over as far as the eye can see with innumerable farm-houses. There is very little of it that is not cultivated. The cotton fields are exceedingly fine, stretching for miles and miles over the level plains. The cotton plants themselves appearing far more productive than those I have formerly seen in the south. According to the natives that I interviewed, this is correct, as the Texas cotton fields are said to produce about twice as much per acre as those in the South Atlantic States. For the accuracy of this statement I will not be responsible, as the average native Texan is exceedingly proud of his state, and very boastful of what it can do.

The meetings of the Convention were very ably presided over by the President, Mr. Chas. S. Martin, who made an unusually efficient presiding officer, and whose ability went far toward expediting business and whose personality injected into the meetings an atmosphere of cordial geniality. It would be difficult to find a more able President than Mr. Martin has proven himself to be.

The newly-elected President, Dr. Wm. J. Schieffelin, is well known to every one connected with the drug business in the United States to-day, and his selection as President of the Association cannot help but be approved by every one who has the pleasure of his

acquaintance. He can be trusted to look upon any matter in a broad, unselfish light, as he is animated by no petty thoughts of personal gain. It is such men as Dr. Schieffelin who help so much to make the National Wholesale Druggists' Association a broad power in the affairs of the country at large, and an association which is known as seeking the public weal rather than its own selfish ends.

Among those who addressed us at the first business session was Dr. Kebler of the Department of Agriculture at Washington. He spoke feelingly against the traffic in cocaine, morphine and opium, and also against those druggists who allow themselves to become mere " booze " sellers, stating that, in his opinion, the drug business should be absolutely divorced from the liquor business. Dr. Kebler made the statement that he believed over 80 per cent. of the morphine and cocaine sold in this country was used for illegitimate purposes, and that 1 per cent. of the people of the United States were habitual users of these drugs in one form or another. He said that he wanted to commend the action of Philadelphia druggists in refusing to sell certain commodities excepting on physicians' prescriptions, and also the National Association of Retail Druggists in putting themselves on record to the effect that they would use every possible effort to enact legislation which would tend to the eradication of those products that are sold indiscriminately to the public, containing cocaine, morphine, opium, etc.

Prof. Eberle, President of the American Pharmaceutical Association, made a very interesting address before the Convention. Among other things, he said that he believed some means could be devised whereby closer association could be established between the A.Ph.A., N.A.R.D., and N.W.D.A., if in no other way than by having a counsel to which delegates from the three associations could be elected.

Mr. Plaut, in replying to Professor Eberle's remarks, paid a very high tribute to the American Pharmaceutical Association and to the excellent scientific work that was effected by the Bulletin of this Association. In alluding to the encouragement which should be given to the American Pharmaceutical Association in its work, Mr. Plaut said that a man of education and of culture, who is efficient and proficient in his profession, is a better customer, pays his bills more promptly, is a more pleasant person to meet, than the mere seller of ready-made medicines. Mr. Plaut also stated that the American Pharmaceutical Association stood very high in Con-

tinental Europe, that its prominent members are well known, its high standing is recognized, and every American who visits foreign pharmacists and foreign laboratories will be surprised to know that very frequently these gentlemen are better known in foreign countries than they are among ourselves. Mr. Plaut urged every one to join the American Pharmaceutical Association, and thus assist in the elevation of pharmacy.

President Martin in his presidential address touched upon many topics of importance to the country at large, which I shall not attempt to repeat, and which are really not capable of being condensed, as they would necessarily have to be, to be included in this paper. Sufficient is it to say that his report showed that the Association has co-operated with many commercial bodies throughout the country and assisted in bringing about important improvements in trade conditions. Mr. Martin advised that the authorities on legislation be instructed to support the passage of an amendment to the Food and Drug Act, adopting the use of the name "Wood Naptha" to take the place of the name "Wood Alcohol," which name is misleading and has often caused death and blindness because of misunderstanding as to the character of the substance. President Martin called the attention of the Association to the fact that the world has reached that stage in its progress when little is accomplished except through organization and united effort, and that the day of small things has passed and it is the duty of all to participate in the organized effort that makes for the good of the whole. He stated that it was not fair, in fact, it was a gross wrong, that the burden of organization be left on the shoulders of the most enterprising and conscientious, while the selfish, the indolent, and those without a proper scruple in appropriating the fruit of other people's labor, remain at home.

The report of the Committee on The Prevention of Adulteration was exceedingly interesting this year, and all those interested in scientific study and the purity of drugs, as they are offered on the markets, should read the report in full. The Committee stated that an eminent expert, who not very long ago uttered in the public prints a rather wholesale denunciation of the traffic in crude drugs on the ground of widespread practices of sophistication, has more recently been quoted as saying that there is no longer one-tenth the adulteration there was formerly. The report then called attention to the indiscriminate looseness with which the words "adulteration"

and "adulterated" are used. These words are employed daily in official utterance, rendered in a way which has robbed them of their original significance. The deliberately corrupted product of the fraud and the cheat when discovered is called "adulterated," and the innocent material which, although absolutely unsophisticated and intrinsically of the highest merit, happens to exhibit some slight defect in respect of a rigidly fixed standard, is condemned by exactly the same formula; it is "adulterated." The element of moral turpitude appears to have been eliminated and must no longer, without proof, be assumed to be present where cases of adulteration are reported. At a later meeting the Association took action on this condition as follows: *Resolved,* That the incoming Committee on Legislation be instructed to take such steps as will bring about, at an early date, the abolishment of the improper use of the words "adulteration" and "adulterated" in the publications of the Board of Food and Drug Inspection, as mentioned at length in the Committee's report. In this connection Mr. Plaut brought up a point which is very important: he called the attention of the Association to the fact that the inspection to which goods are subjected at the various points of entry are anything but uniform. He mentioned a case where asafetida bought in Hamburg and sold to a house in Philadelphia was entered at the port of Cleveland, and stated that other drugs were being entered at such points as Minneapolis, Cleveland, Ogdensburg, Albany, etc., where there were no thoroughly organized Bureaus, equipped to test the quality of the drugs, and that in this way inferior drugs obtained admission to the country in a way that could not be effected were they entered at some of the regular ports of entry. He advised that the members use their efforts to abolish this objectionable condition of affairs. Mr. Plaut also brought to the attention of the Association the present method of printing the court decisions in the case of prosecutions brought by the Department of Agriculture. As they are printed they are sent broadcast over the country, and it is necessary often to read the leaflet from beginning to end before the reader finds out whether the defendant is innocent or guilty. Many people read but the first few lines and are left with a false impression that the defendant has committed a crime, whereas often the last few lines would prove that he was absolutely innocent. Many delegates recognized the truth of this contention, and a resolution was passed requesting the Committee on Legislation to look into the

possibility of having the decisions in which the defendant is not proven guilty published in a form different from that in cases in which he is convicted, or else that no notice be issued in such a case. To return to the report of the Committee on the Prevention of Adulteration, the report also contends that under the operation of the law, dealers are purchasing goods under a U.S.P. label for resale, even though they know, or suspect that such goods are not what they exactly seem to be, and that they smother their true beliefs by the expression, "What is it to me what the bottle actually contains, does it not bear the guaranty of a reliable house?" The Committee contends that the purchasing departments can do much to prevent adulteration by curbing this insidious tendency. The Committee believes that the work of the Government inspectors employed in inspecting the quality of important drugs has undoubtedly become more and more effective. There is still, however, they believe, a great deal of inconsistency in the methods employed and too strong a tendency to be over-technical in the application of the law to cases where there is obviously no sophistication or demerit. It will be necessary for me to pass over the details of the balance of the report, because they are many and would take too long to read at this time.

The report of the Committee on Trade-marks contained much of interest. The case of the manufacturers of the "Keep Clean Brushes" against the manufacturers of the "Stay Clean Brushes" was cited, in which it was found that, though neither word was capable of being trade-marked, because a descriptive word cannot be trade-marked under our present law, nevertheless, under the laws of unfair competition, the manufacturers of "Keep Clean Brushes" were enabled to obtain a judgment against the manufacturer of "Stay Clean Brushes," because (I quote from the decision) "Where the defendant has so dressed his goods that they may be mistaken for the goods of the complainant, his motive in so doing is either honest or dishonest; if honest, he should stop voluntarily, if dishonest, he should be compelled to stop." The Committee called attention to the Trade-mark Law in California, under the terms of which the manufacturer, in order to protect his rights within the state, must register his trade-mark with the state authorities. A test case is being brought to prove this law unconstitutional, but in the meantime the manufacturers are advised to register their trade-marks in order to fully protect their rights.

The Committee on Paint, Oils and Glass, the advisability of continuing which had been questioned the previous year, proved its worth by coming forward with an excellent report, including many points of undoubted interest and value. The Hepburn Paint Bill was discussed, but what will interest this meeting more was that part of the report of the Committee which has to do with turpentine. Under the Pure Food and Drugs Act it would be necessary for turpentine, or spirits of turpentine, to be unadulterated and to answer the U.S.P. requirements, or else to be properly labelled. Under the ruling whereby an article of this character can be labelled "For technical use" the dealers are enabled to sell an adulterated product without fear of prosecution. Hiding behind this regulation, a large traffic in adulterated turpentine has been carried on, and no dealer to-day can be absolutely sure he is dispensing pure spirits unless he either tests the goods himself, or knows personally that the dealer from whom he buys is absolutely honest. There are three common adulterants: First of all, spirits of turpentine is distilled from the dip or scrape of the living pine tree. The first adulterant, pure wood spirits of turpentine, is made by the destructive distillation of the wood; another adulterant is common benzine; still a third is composed of high boiling hydrocarbons analogous to benzine. Pure wood spirits naturally forms an excellent adulterant, due to the fact that it is very similar in physical properties. Common benzine is the poorest adulterant, on account of its odor and physical properties. The high boiling hydrocarbons, being odorless and very similar to turpentine in physical properties, make an ideal adulterant. Twenty-three samples, most of them obtained from suspected sources, were analyzed by the Committee. Out of the 23 tested, 17 showed adulteration; the average amount of adulterants being 30 per cent. The greatest amount of adulteration was found in Russian turpentine, which contained no trace of turpentine at all, being petroleum. The lowest amount was 10 per cent., this being the percentage usually put in by several unscrupulous dealers in New York City, who sell their product as "pure spirits of turpentine." The quotations of these dealers are always a cent or two under the Official Naval Stores prices. Another group of turpentine adulterators, using about 35 per cent. petroleum, made their headquarters in Cleveland, Ohio. One firm is quite clever, guaranteeing their product to be "pure" according to the analysis printed on the head of the barrel, and not stating whether it was pure turpentine or pure

benzine. The State of Ohio recently passed a Pure Turpentine and Linseed Oil Act which has caused much annoyance to the dealers in adulterated products in that state. The Committee recommends the enactment by each state of a similar law. I made a study of this law, which at first seemed very drastic, but on further consideration, every detail can be lived up to by an honest man doing an honest business and will work no hardship on any one who comes under this heading. The law states that no one shall sell under the name of turpentine, or spirits of turpentine, or any compounding of the word "turpentine," or under any name or device illustrating or suggesting turpentine or spirits of turpentine, any article which is not wholly distilled from rosin, turpentine, gum, etc., and unmixed and unadulterated with oil, benzine, or any other foreign substances of any kind whatsoever, unless the package be marked with letters not less than 2 inches high, "Adulterated Spirits of Turpentine." It can be readily seen that this law covers the situation nicely, and Pennsylvania would do well to adopt such a law, and I recommend that you, whenever the opportunity presents itself, speak a word in favor of such legislation. I would be glad to supply any number of copies of the Ohio law to those who would like to study it. The Chairman of the above-mentioned committee, Mr. Levi Wilcox, of Waterbury, Conn., deserves high commendation for his very excellent report.

The report of the Proprietary Committee, of which Dr. Schieffelin was Chairman, contained considerable of interest to the trade. The general tendency, the Committee reported, of decisions rendered by various courts throughout the land, was to take a less drastic position with reference to the violation of the Sherman Anti-Trust Law. Two cases were referred to in this country and one in Canada where the court took the position that the manufacturer had the right to insist upon the maintenance of his retail price where it could be shown that such an action is only incidentally and indirectly to resist competition, while its chief result is to foster the trade and increase the business of those who make and operate it. These decisions, so different from the one rendered at Indianapolis in the case of the United States against the drug trade, tend to increase confidence in the stability of business and encourage manufacturers to spend larger amounts in advertising their goods, because they feel that they can protect their interests by being allowed to maintain their price to the consumer. An important decision was cited which

increases the value of the guarantee, and shows that the courts will accept a chain of guarantees as fixing the blame on the original guarantor, and that he will be held responsible for fraud even though technicalities may be brought to bear on the case. The case in question is one in which a manufacturer sold to a wholesaler in the same state and the wholesaler in turn sold to a retailer in a nearby state. The manufacturer attempted to evade responsibility on the ground that his sale was only one within the state, rather than an interstate sale, but the courts decided otherwise. The report calls attention to the National Insecticide Act, which was intended to go into effect on January 1st, 1911, and with which you are probably familiar; if not, you had better send for a copy of the Act, as its provisions are more inclusive than you would at first think. The definition is exceedingly broad, and covers insect powders, powdered white hellebore, and every drug or preparation, proprietary or otherwise, which is intended to exterminate insects of all kinds. It also includes fungicides. A committee was appointed by the three secretaries to formulate regulations for the enforcement of the Act, which committee has not yet reported the nature of these regulations, therefore, all dealers have been obliged to hold up the printing of their labels until such regulations are promulgated, because otherwise it might be necessary for them to make two changes in order to comply with the law. Dr. Schieffelin commented on the Owens' Bill, which provides for the establishing of a National Department or Bureau of Health. He stated that his committee opposed that portion of the bill which gives the proposed department power to establish standards for chemicals and other drugs, because they took the position that this was unnecessary, as the present arrangement, which makes the United States Pharmacopœia and National Formulary the official standard, is sufficient. There is no question that the National Department or Bureau of Health could utilize the vast resources of the Federal Government to the great advantage of the nation, by gathering and disseminating information, and materially assisting in preventing diseases and preserving the health of the people. He believes this could be done without encroaching upon the constitutional prerogative of states to exercise police power within their respective borders. The health of our people is the greatest asset of the nation, and any feasible plan that will minimize the loss of valuable human lives is worthy of the most careful consideration.

The report of the Committee on Legislation, whose Chairman is Mr. Chas. A. West, of Boston, shows that they have done much valuable work during this period when it seems to be every politician's ambition to invent some new provision whereby the drug trade can be better controlled. The work of this committee is exceedingly arduous, and it would be practically impossible for the Chairman to operate effectively in every state in the Union, were it not for the fact that the individual members in the states themselves willingly furnish their co-operation. One of the bills mentioned by this committee that is now before congress, was introduced by Mr. Moore of Pennsylvania. It provides for the labelling of packages containing foods, beverages, and drugs, and makes it necessary that they should show the weight or measure on the label. That such a requirement should be made in the case of drugs, whose value does not depend by any means on their weight or measure, is manifestly ridiculous, and the bill has been opposed by the committee. It seems likely that in its present form it will not be passed, but that it will be revised and be made more comprehensive, because as at present worded it only covers the District of Columbia. As the bill is at variance with several state laws pertaining to weights and measures, if passed, it will cause a great deal of confusion. The Committee calls the attention of the Association to the fact that the Pure Food and Drugs Acts passed in the various states are very similar. The attempt to carry out the law by making rules and regulations has proven rather disastrous. The individual who is given the power to make such rules and regulations often largely exceeds his authority, or else insists upon minor points of detail, which, because they differ in the different states, make interstate transactions exceedingly difficult. A label which will comply with the National Law often will not comply with the state regulations, and if it does comply with the regulations of that state, will not comply with the regulations of other states. It must be remembered that the law is a law to prevent adulteration and misbranding only, and that the final word as to whether goods are mislabelled or not is to be decided on those two points only. The Committee requests that the members attempt, as far as possible, to counteract this tendency toward the issuing of annoying regulations, and, in the opinion of the committee, this matter requires some positive action on the part of the united drug interests.

The Legislative Committee reports much activity along the line

of narcotic legislation. This seems to have become a favorite subject for new bills. Three important ones are now under consideration; the Mann Bill, the Collum Bill, and the Foster Bill. The Mann Bill requires that all sellers and shippers of habit-forming drugs shall keep an exact record, regardless of what the shipment may be, and requires a record of such shipment to be kept by the receiver. A number of minor points in the bill seem calculated to work injustice, and the committee, therefore, considers that this Bill should be revised before it receives the support of the drug trade. The Collum Bill was introduced in the Senate, but being a revenue measure, was rejected, as such legislation could only originate in the House. The Foster Bill purposes to place the control of the traffic in narcotic drugs in the charge of the Internal Revenue Department. In order to accomplish this purpose it provides that every wholesale dealer and retail dealer shall be registered, and no sale shall be made excepting to those who have been properly registered. A fine of $500 or imprisonment for one year is the penalty for shipping to any one not properly registered. It also provided for an Internal Revenue tax of 5 cents a pound or fraction of a pound on opium, chloral, and cannabis, and 1 cent a pound on coca leaves. A number of methods of keeping the accounts are provided. The plan to carry out the Internal Revenue control is to put on a stamp, sealing the package, before it is released from a bonded warehouse. The general attitude of the committee is that this measure would be exceedingly burdensome and that it might be possible to accomplish the result in some way less burdensome. Mr. Hamilton Wright, the United States Opium Commissioner, pledged himself to the passage of some bill regulating the traffic in opium, when he was a delegate to the International Opium Congress. He, therefore, considers that, in order to keep faith with the Congress, it is exceedingly desirable that some legislation should be passed in the near future. He is somewhat in favor of the Foster Bill, but not definitely committed to its passage. The representatives of the N.W.D.A. have attempted to persuade him that if this measure should be passed it should be made applicable to cocaine alone at first, until the measure is tried out. This suggestion Mr. Wright has under consideration. There is 400,000 lbs. of opium imported into the United States in a year. Of this it is estimated 300,000 lbs. is used for purposes other than medicine. This figure is very high as compared with the amount consumed in other countries where they have effective laws

governing the traffic in narcotic drugs. The Committee reports that in the case of the Pure Food & Drugs Act it is pretty generally acknowledged by those most familiar with the workings of the law, even including officials, that the labelling clauses are rapidly losing effectiveness, especially so far as the public is concerned. The public does not read the labels or does not understand what it does read. This opinion is so generally accepted that there are many who hope for the enactment of laws that will compel the manufacturers to put in his advertisements all that the law compels him to put on his label.

One thing more I think worth mentioning: the following resolution was passed by the Association: WHEREAS, The attention of the N.W.D.A. has been called to the fact that efforts are now being made to change the form, style, and spelling of the articles used as drugs and chemicals in the coming revision of the U.S.P., be it therefore, *Resolved,* That this Association protests against any changes in form, style, and spelling, except those which may be necessary in the few cases where more exact information and research requires a change. The resolution was introduced because the Association was informed that certain parties were bringing pressure to bear to have the form, style, and spelling of the Pharmacopœia changed. It requires no argument to prove to you what a mistake this would be.

In closing, I would say, that the meeting at Dallas was an entire success, and the members of the Association expect to spend at least another year working in perfect accord toward the betterment of conditions in the drug trade without any factional quarrels to mar the effectiveness of their work.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

BY M. I. WILBERT, Washington, D. C.

Few subjects, now before the retail druggists of this country, have received more widespread attention by the pharmaceutical press than the *Foster anti-narcotic bill* which is being considered by the Ways and Means Committee of the House of Representatives.

This bill is practically a duplicate of the Cullom bill which was considered in the Senate last year, and as now worded is designed to regulate traffic in cocaine and other habit-forming drugs by imposing an internal revenue tax and requiring that detailed records of all sales be made and reported to the Commissioner of Internal Revenue who is also to make regulations for the enforcement of the act.

In the hearings that have been held on this bill it was generally admitted that the abuse of habit-forming drugs had spread to an alarming extent, in the last 20 or 30 years, and that their consumption, at the present time, was not accounted for by any legitimate use to which they could be put.

It is also agreed that the only way by which the several State laws regulating the sale of habit-forming drugs could be enforced was by having an authoritative source of information regarding the sale, in a large way, of the several articles that are involved.

It must be admitted that this law, or any law of a similar nature, will entail hardships and will involve the expenditure of time and money on the part of those engaged in the several branches of the drug business. But, on the other hand, the possibility of removing from the drug trade the stigma of debasing all strata of society by the encouragement of drug habits is one that should and no doubt will atone for all the trouble and expense that can possibly be involved.

Public Health Service.—Legislation looking toward the protection of the public health has also been discussed at length and some progress has been made toward the solution of the problems involved. The report of the Committee on Interstate and Foreign Commerce, indorsing the Mann bill, to change the name of the Public Health and Marine-Hospital Service to the Public Health Service and defining its field of usefulness, is reprinted in the *Oil and Paint Reporter* (February 6, 1911, p. 40) and pharmacists who are interested in the progress of public health legislation should read this report and consider the possibilities involved.

Ph. Germ. V.—In Europe the new "Deutsches Arzneibuch" has been probably the most fruitful topic of discussion. This book while much larger than any of its predecessors contains but a total of 43 more titles than the Ph. Germ. IV. It represents a rather radical change in the method of revision in that it is the direct product of the "Reichs Gesundheitsamt," being compiled by the

division on materia medica. This division consists of two subdivisions, one medical and one pharmaceutical, and the work on the pharmacopœia represents the contributions of 26 experts.

An editorial (*Pharm. Zentralh.*, 1910, v. 51, pp. 1177–1179) points out that the new Ph. Germ. has a decidedly broader field of usefulness than its predecessor and that the concise and altogether limited descriptions of the former editions have been replaced by more complete monographs, which will be found to be of value not alone in the pharmaceutical laboratory but also in the use of the book by students and by physicians who will find in them much information of practical value.

The general formulas were increased by 13, viz., bacilli, cerata chartæ, collemplastra, mucilagines, pastæ, pulveres, mixti, sapones medicati and vina medicata.

The provisions of the Brussels protocol have been adopted with the special designation P. I.

With the titles adeps suillus, sebum ovile, spiritus e vino and vinum no descriptions or tests are appended, and these articles are expected to conform to the requirements made for commercial articles.

Trademark Names.—A review of the new German Pharmacopœia points out that the repeated occurrence of protected designations in the list of additions will surprise those who have followed even superficially the recent trend of events in Germany. It has been the aim of the responsible authorities so far to avoid in any way recognition of vested rights, and thus in the last edition the German pharmacist was regaled with the appalling scientific appellations for antipyrin and salipyrin. In the draft of the present edition, this attitude was adhered to, and the full chemical designation of novocaine and stovaine, for instance, figured as the only titles to the respective monographs. The explanation of this *vollte-face* is not without interest and piquancy. We are told that where the scientific designation is more convenient or in general use it has been adopted; in other cases the protected name was chosen for the title, followed by the chemical name and the protected name also appears beneath the scientific title as a subtitle. The adoption or mention of the registered appellation, however, merely indicates that the *protected preparation must in every respect fulfil the requirements set forth in the Pharmacopœia.*—*Chem. and Drug.*, Lond., 1910, v. 77, p. 899.

Post-Graduate Instruction.—The Pharmaceutical Institute of

the University of Strassburg announces that a post-graduate course of instruction, covering the changes and requirements of the Ph. Germ. V., is now being arranged for. The course is designed as a review of the more important tests and assay methods of the pharmacopœia and will consist of lectures, demonstrations and practical laboratory work.—*J. d. Pharmacie v. Elsass-Lothringen,* 1911, v. 37, p. 292.

British Pharmacopœia.—Edmund White, in resigning as a member of the British Pharmacopœia Committee of Reference in Pharmacy expresses himself as being dissatisfied with the progress that is being made in revising the British Pharmacopœia. He thinks conditions existing in connection with the revision of the British Pharmacopœia are quite unsatisfactory and points out that the German Pharmacopœia, which is now a State publication, has been developed along much more satisfactory lines.—*Chem. & Drug.,* London, 1911, v. 78, pp. 186–187.

British Pharmaceutical Codex.—An editorial asserts that the revision of the British Pharmaceutical Codex is now well advanced, though it may be several months before it approaches completion. The editorial also points out that most gratifying responses have been received from all to whom appeals for assistance have been made and the Codex as revised may therefore be depended upon as representing the consensus of opinion of practicing pharmacists throughout Great Britain.—*Pharm. J., London,* 1911, v, 86, p. 2.

The Codex Revision Committee is regularly publishing suggested new formulæ and alterations with the request that they be reviewed by pharmacists and that criticisms and further suggestions be forwarded to the office of the committee. These published formulæ have elicited considerable comment, and it is expected that the book as finally published will be free from the glaring errors usually found in works of this kind.

International Congress of Applied Chemistry.—William H. Nichols (*Science,* 1910, v. 32, p. 689) discusses the origin and development of the International Congress of Applied Chemistry, and calls attention to the need for making active preparations for the eighth international Congress which is to meet in this country early in September of 1912.

John Morgan.—A news note announces that at a meeting held in the office of the Provost of the University of Pennsylvania, on

January 13, it was decided to erect a suitable memorial to Dr. John Morgan, the founder of the medical department of the University, the originator of medical schools in the United States, and the first physician, in America, to introduce the writing of prescriptions.—*J. Am. M. Ass.*, v. 56, p. 205.

Paris School of Pharmacy.—Professor Guignard, who desires to devote himself hereafter solely to scientific work, has requested the minister of public instruction to relieve him of the directorship of the higher school of physiology and pharmacy, which he has carried on for about 15 years, having succeeded Professor Planchon. The faculty of the school has unanimously elected, as the new director, M. Henry Gautier, professor of inorganic chemistry at the school.—*J. Am. M. Ass.*, 1911, v. 56, p. 130.

Medical Curriculum.—An editorial note (*Chem. & Drug.*, Lond., 1910, v. 77, p. 834) quotes the *Lancet* which suggests that the reaction against studying materia medica in the medical curriculum has gone too far, and although it is hopeless to attempt to reintroduce the old materia medica a modified form should be tried, and outlines a course that might well be adopted in British medical schools.

Progress in Pharmacology.—An editorial commenting on the programme of the Section on Pharmacology and Therapeutics of the British Medical Association asserts that pharmacists, if they are to keep up to date, must keep in close touch with that branch of medicine which deals with the study of the composition and uses of remedies of medicinal value and they must therefore know about the shifting of the old landmarks and note the progress which pharmacologists make in elucidating the action of medicinal agents.—*Chem. & Drug.*, Lond., 1910, v. 77, p. 832.

Antityphoid Vaccination.—George B. Foster reports an instance illustrating the efficacy of antityphoid vaccination in the U. S. Army. Of 92 members of Company A, First Battalion of Engineers, who were vaccinated, not a single case of typhoid fever developed, while of the total of 24 men not so protected six, or 25 per cent., developed typhoid fever.—*J. Am. M. Ass.*, 1910, v. 55, pp. 1808–1809.

Essential Oils as Antiseptics.—An editorial in discussing the use of essential oils as antiseptics points out that essential oils or substances containing them are the oldest antiseptics that have been used by man, but that it is only within recent years that any

systematic study of their antiseptic action has been made. In a recent investigation made by W. H. Martindale to determine the carbolic acid coefficient of each oil or aromatic substance studied, it was found that oil of origanum had upwards of 25 times the coefficient of carbolic acid; thymol and carvacrol were found to be nearly as active as oil of organum, the coefficient figures being 25.29 and 21.32 respectively.—*Chem. & Drug.*, Lond., 1910, v. 77, p. 832.

CHEMISTRY OF THE TERPENES AND CAMPHORS.—Joseph Samuel Hepburn, in a recent number of the *Journal of the Franklin Institute* (February, 1911, v. 171, pp. 179–203), presents an interesting review of the work that has been done by Otto Wallach and his students on the chemistry of the terpenes and camphors and their related compounds. As many of the compounds referred to are official or at least common articles in the average drug store, this review will be found to be of unusual interest to pharmacists who are desirous of learning the relations existing between them.

STIRRING ROD.—An abstract (from *Südd. Apoth.-Ztg.*, 1910, p. 622) points out that glass tubing properly sealed at either end makes a much better stirring rod than a solid glass rod. The resulting rod is lighter, has a greater volume, and, as a rule, does not break so readily, even when dropped on a wooden table.—*Schweiz. Wchnschr. f. Chem. u. Pharm.*, Zurich, 1910, v. 48, p. 765.

MELTING-POINT DETERMINATION.—Atherton Seidell describes and illustrates a convenient arrangement for providing constant stirring of the sulphuric acid or other bath in making melting-point determinations. The mechanical stirring device is driven by a small water motor, while an even heating of the bath is insured by protecting the flame from air currents and by preventing the free flame from coming in contact with the tube containing the bath.—*J. Am. Chem. Soc.*, 1911, v. 33, p. 83.

DROPS.—Wulff and Hillen describe and illustrate a normal drop ampoulle which they believe to be particularly well adapted to serve as the normal drop counter provided for by the Brussels Conference Protocol.

The apparatus can be used for dispensing substances that are to be used in drop doses, particularly solutions to be used in the eye, where sterility is considered to be an important factor.—*Apoth. Ztg.*, Berl., 1909, v. 25, p. 1014. See also *Pharm. Post*, 1911, v. 44, p. 53.

SALVARSAN is the name under which "606" is being marketed

in this country. A number of papers on the chemical and pharmaceutical properties of this substance have appeared in the current journals and the information necessary for preparing the material for injection is available from the literature accompanying the package.

A report on the chemical properties of salvarsan, by W. A. Puckner and W. S. Hilpert (*J. Am. M. Ass.,* 1911, v. 55, p. 2314), contains the following popular description of its behavior: "Salvarsan is an arsenic compound containing that metal in a low state of oxidation and the product is, therefore, a powerful reducing agent and is decomposed by bodies which are oxidizers, including air. Being a weak base its hydrochloride, when dissolved in water, is largely decomposed by the latter (hydrolyzed) and hence gives a solution having an acid reaction. A solution of salvarsan is therefore acid and will remain so until for every molecule of salvarsan there have been added two molecules of sodium hydroxide or a similar monovalent base."

William Allen Pusey, in a discussion of the situation regarding salvarsan, asserts that indications are very strong that we are on the verge of a period of indiscriminate and reckless use of this remedy that will result in disappointment and damage to many patients. He further points out that this drug does not absolutely cure syphilis and that in the hands of careless or incompetent practitioners it is likely to do much harm.—*J. Am. M. Ass.,* 1911, v. 51, pp. 118–120.

A recent number of *N. A. R. D. Notes* (February 2, 1911, p. 998), calls attention to an advertisement from the *Chicago Sunday Examiner* of January 23, 1911, in which salvarsan ("606") is being indirectly exploited to the laity. Needless to say advertisements of this type are destined to do an untold amount of harm.

Joha is the name applied to an oil solution of salvarsan that is said by its promoters to be quite stable. It is being marketed in Germany, in ampoulles containing the equivalent of 0.4 and 1.2 Gm. of salvarsan.—*Pharm. Zentralh.,* 1911, v. 52, p. 21.

Adalin is the name given to brom-diethyl-acetyl urea. This substance occurs as a colorless, nearly tasteless powder that is only sparingly soluble in cold water but freely soluble in alcohol. Adalin is being recommended as a bromide and is given in doses of from 0.3 to 1.0 Gm. three times a day.—*Pharm. Post,* 1911, v. 44, p. 84.

Adipol is said to be a preparation of mineral fats that is permanent and has the property of absorbing upwards of 30 per cent. of water.—*Pharm. Zentralh.,* 1911, v. 52, p. 52.

Adrenine.—Macadie, W., discusses the coloration of solutions of adrenine (adrenalin) and records a number of experiments made by him to prevent the development of free ammonia which he believes is the causative factor. He has found chloroform to be the most efficient antiseptic and recommends keeping a layer of chloroform at the bottom of the solution of adrenine, which is to be kept in dark amber-colored bottles.—*Pharm. J.*, Lond., 1910, v. 85, p. 660.

Afridol.—An abstract asserts that afridol, which is recommended as a powerful antiseptic and disinfectant, is an orthotoluate of mercury and sodium of the formula $(C_6H_3)(CH_3)(CO_2Na)(HgOH)$. It is especially recommended as a component of antiseptic soaps for disinfecting the hands and instruments in the course of surgical operations.—*Chem. & Drug., Lond.*, 1910, v. 77, p. 828.

Aspirin.—Cyrus Graham reports a case of acute intoxication following the ingestion of two five-grain tablets of aspirin. The poisoning resulted in marked œdema of the mucous membranes of the eyes, nose and mouth; to such an extent that the patient could hardly breathe. There was also considerable swelling of the head and neck, congestion of the conjunctivæ and impairment of vision. The symptoms disappeared in from ten days to two weeks, but Dr. Graham nevertheless believes that aspirin should be listed as one of the dangerous drugs and should not be retailed indiscriminately to the laity.—*J. Am. M. Ass.*, 1911, v. 56, p. 261.

Calmine is one of the names under which veronal-sodium, a combination of diethyl barbituric acid and sodium, is being exploited as a new and absolutely safe hypnotic. The same substance is also being marketed as medinal and pharmacists need not be surprised to find that thoughtless physicians will combine calmine, medinal and veronal in the same prescription.—*J. Am. M. Ass.*, 1911, v. 56, p. 137.

Digitalis.—J. Gordon Sharp and J. Lancaster, in a general discussion on the time of gathering digitalis and the keeping qualities of the tincture, present a number of observations on this important drug. They have found that the leaves from wild growing plants are frequently contaminated by other leaves. They also point out that the leaves themselves, if thoroughly dry are more permanent than is the tincture.—*Pharm. J.*, Lond., 1911, v. 86, pp. 102–104.

Xrayser II, in a reference to the history of digitalis, points out that this drug is receiving a degree of attention which is in strong contrast with the neglect it suffered for a century and a half after

its first introduction into the Pharmacopœia in 1650, and expresses the hope that the time is not far distant when its active constituents will be scientifically determined, and their respective value more accurately ascertained.—*Chem. & Drug.*, Lond., 1910, v. 77, p. 861.

J. Burmann has published (*Bull. Soc. Chim.*) a criticism of Keller's method of estimating digitoxin, and says it can only be regarded as valid if it is admitted that the product weighed always contains true digitoxin in the same proportion relative to the other glucosides present. He gives the following toxic doses per kilogramme of body-weight of rabbits: Merck's crystalline digitoxin, 0.0026 Gm.; digitoxin prepared by Keller's method of estimation 0.008 Gm.; or 9.2 c.c. of a 0.3 per cent. solution in alcohol (7 parts), glycerin (25 parts), and water (68 parts); Cloetta's soluble digitoxin, 10.3 c.c. of a 0.3 per cent. solution in the triple menstruum just mentioned.—*Chem. & Drug.*, Lond., 1911, v. 78, p. 48.

ETHYL CHLORIDE.—Horatio C. Wood, Jr., reports a statistical study on the comparative danger of ethyl chloride as an anæsthetic. He finds that the approximate mortality from the use of ethyl chloride is 1–6000 anæsthesias while the mortality for nitrous oxide is about 1–1,000,000, chloroform 1–3500, and ether 1–15,000 anæsthesias. As the use of ethyl chloride corresponds more nearly to that of nitrous oxide, Wood concludes that it must be considered as an unsafe anæsthetic.—*J. Am. M. Ass.*, 1910, v. 55, p. 2229.

FORMUROL.—The Secretary of the Council on Pharmacy and Chemistry of the American Medical Association reports a chemical examination of formurol which corroborates the findings of Zernik that formurol is not a definite chemical compound but is in reality a mixture of hexamethylenamin and sodium citrate.—*J. Am. M. Ass.*, 1911, v. 56, p. 210.

GLOBULARIN is the name given to a glucoside obtained from *Globularia alypum*. It is said to cause an increase, followed by a transitory decrease in the amount of urine excreted.—*Pharm. Zentralh.*, 1911, v. 52, p. 52.

GLYCERIN.—An editorial in the *Journal of Industrial and Engineering Chemistry* (January, 1911, v. 3, p. 3) points out that the manufacture of nitroglycerin explosives is the determining factor in regulating the price of glycerin. From being a by-product in the manufacture of lead plaster glycerin has become one of the principal products of the saponification of fats and at the present time sells at from two to three times the price of the raw material from which it is made.

HELENIC ACID.—Reeb (*Nauveaux Remèdes,* 1910, 511) has extracted from the leaves and flowers of *Helenium autumnale* a crystalline glucoside of the formula $(C_8H_{10}O_2)x$. It melts at 161° and is of an acid nature, and has therefore been named helenic acid. On hydrolysis it yields glucose and a body not further examined.—*Chem. & Drug.,* Lond., 1911, v. 78, p. 48.

L-SUPRARENIN SYNTHETIC is epinephrine produced synthetically according to the method of Stolz and Flaecher (*Ztschr. f. physiol. Chem.,* v. 58, p. 189). It occurs as a white odorless powder nearly insoluble in water, alcohol and ether. It melts at 211 to 212° C., and, as its name indicates, has the power of rotating polarized light to the left. This substance has the chemical and physical properties and produces the physiologic effect of natural epinephrine obtained from suprarenal glands.—*J. Am. M. Ass.,* 1911, v. 51, p. 120.

L-SUPRARENIN SYNTHETIC BITARTRATE is the acid tartrate of l-suprarenin synthetic. It occurs as a white odorless powder readily soluble in water, yielding an acid solution. It melts at 149° C. and rotates polarized light to the left.—*Ibid.*

NIEMEYER'S PILL.—James Tyson asserts that the name "Niemeyer's Pill" is being erroneously applied to the well-known pill of calomel, squill and digitalis. This pill antedates Niemeyer, and if known by any name it should be that of Addison or Guy.

The true Niemeyer pill is composed of one grain of quinine, one-half grain of digitalis and one-quarter grain of opium, and was used by that physician for the fever of pulmonary tuberculosis.—*J. Am. M. Ass.,* 1911, v. 56, p. 211. See also p. 443.

PHENOLPHTHALEIN, ACTION OF.—Fritz C. Koehler reports an experiment made upon himself, to determine the factors influencing the action of phenolphthalein as an aperient. He found that while 0.10 Gm. of phenolphthalein had a distinctly laxative action under ordinary conditions and when the feces reacted alkaline a much larger dose had no effect when the diet was regulated to produce an acid reaction of the feces.—*Schweiz. Wchnschr. f. Chem. u. Pharm.,* 1910, v. 62, p. 802.

POPPY.—M. G. J. M. Kerbosch reports a comprehensive study to determine where and when the important opium alkaloids are formed in the growing plant. He concludes that seeds of *Papaver somniferum* L. contain a trace of narcotine and amorphus alkaloid. The germinating seeds have an increased narcotine content and the

sequence in which the alkaloids are found in the growing plant is narcotine, codeine, morphine, papaverine and thebaine. The first four of these alkaloids occurring in plants that are from 5 to 7 cm. high.—*Arch. d. Pharm., Berl.*, 1910, v. 248, pp. 536–567.

The Phosphorus Match.—A recent editorial in the *Journal of Industrial and Engineering Chemistry* (January, 1911, p. 1) contains some rather interesting information regarding the origin and development of matches and the dangers attending the exposure to fumes of phosphorus. The earliest known matches, made in 1812, were tipped with potassium chlorate and sugar and ignited by sulphuric acid. The phosphorus match was introduced by Derosne in 1816, and because of the danger attending its manufacture has been prohibited in nearly every European country, preference being given abroad to the so-called safety matches or to matches tipped with a composition containing one or the other of the sulphides of phosphorus.

PHILADELPHIA COLLEGE OF PHARMACY.*

By Howard B. French, President.

Since the world began the inspiration of association has stirred the hearts of men, enlightened their minds, strengthened their hands and ennobled their lives. The spirit of great acts lives throughout the years, creating and forwarding movements which bless mankind.

When the climax of the long night of colonial injustice and oppression had been reached, and the representatives of a suffering people came together in 1774, to consider ways and means of relief, they wended their way to a spot already historic, where the fires of liberty had been lighted and where the voice of the coming nation of freemen had been heard, demanding just recognition of the inalienable rights of man. As though directed by the finger of fate, building better than they knew, a few years before, in 1771, a little company of men, drawn from the humbler walks of life, in the City of Penn, honest and faithful toilers,

*An address covering some of the interesting facts in the history of the College and delivered at a banquet given by the president at the Union League Club, Philadelphia, in commemoration of the ninetieth anniversary of the College, February 23, 1911.

helping to lay the foundation and build the superstructure of a mighty republic, had reared a meeting place which was now to become the scene of events memorable while time shall last.

Very few of the delegates to the Carpenters' Hall Assembly knew or had ever heard of this unpretentious building, modestly located back from the main street of the city, as though seeking an undiscoverable retreat. From the Colonies far and near, they came, and under the guidance of the God of nations, whose protection they wisely and devoutly sought at the very beginning, they solemnly and courageously deliberated. Their just and patriotic conclusions met with an instant and hearty response in the hearts of the people. They made Carpenters' Hall a Mecca for unborn generations, a place where the men of the future might safely seek counsel and wisdom.

As the present representatives of an honored and beneficent institution, it is our privilege to remember with pride and satisfaction the fact that its founders first met where the patriotic leaders of revolutionary days first assembled. It could not have been otherwise than that they too should have built wisely and well.

During the fifty years of its existence, from 1770 to 1820, before its temporary occupancy by the founders of the Philadelphia College of Pharmacy, Carpenters' Hall had a peculiarly eventful history. It had its singular vicissitudes, and at one time was nearly lost sight of as a place worthy of lasting public honor. Yet within that period, it was the scene of events of surpassing importance. The Provincial Assembly of Pennsylvania met there in July, 1774, and in September and October of the same year, the first American Congress. In 1775 a conference was held in this Hall of far-reaching effect upon the development of trade and commerce in America. This was an assemblage of prominent financiers and manufacturers interested in the establishment of the cotton and woollen industry in this country. The following year, in 1776, the Provincial Committee met and resolved to call a convention to form a government for Pennsylvania, which should receive all its authority from the people only. When, liberty having been achieved, the problem of the hour was the formation of a national government which should stand the storms and trials of the years to come, here again, in 1787, came the chosen counsellors of the people to frame that immortal document—the Con-

stitution of the United States—which the greatest Englishman of the nineteenth century declared the wisest instrument ever conceived by the mind of man. In 1791, the first Bank of the United States commenced business in Carpenters' Hall, continuing therein for six years.

With extraordinary self-forgetfulness, it was at this time, the company owning the Hall, now so historic and sacred, withdrew from it, so far as their meetings were concerned, and for two generations met in an adjoining building. The Bank of the United States was succeeded, in 1797, by the Bank of Pennsylvania, for a short period. From 1802 until 1817, the Federal government there collected its custom duties. After this came the second Bank of the United States. Successive occupants in different parts of the building represented the literary, scientific, benevolent, educational and musical interests of the city.

For a time Friends met in the Hall for worship, consecrating its wall to spiritual things. In 1833 the Supreme Court of Pennsylvania held its sessions in this building. In 1859 City Councils sought to purchase the Hall, on account of its historic interest and association, but the proposition was respectfully declined. Having been carefully restored and maintained in its primitive simplicity, the old Hall has been in sole possession during the past sixty years of the Carpenters' Company. Its history should ever inspire men to unselfish purposes and lofty deeds.

The spirit which actuated the founders and early trustees of the Philadelphia College of Pharmacy is most impressively illustrated on the pages of the minute books of the institution. These earnest minded men never lost sight of the great objects to be attained, the correction of trade abuses and the elevation of their calling, the extension of knowledge and the consequent inestimable service to mankind. One of the first matters considered, following organization, was careful revision of the existing pharmacopœia, in accordance with the latest accepted standards, every formula to be satisfactorily tested before approval. Exceeding care was exercised in the election of members of the association and in the selection of trustees and members of the faculty of the College. Only men of the highest intelligence and recognized probity were entrusted with the direction of its affairs. The name was early changed from the Philadelphia College of Apothecaries to the Philadelphia College

of Pharmacy. Evincing an earnest desire for the newest information on trade and professional subjects, at a meeting in December, 1822, a subscription of $25 to the best periodicals relating to pharmacy was authorized. At the same meeting, the Board of Trustees presented an encouraging report of the work of the College during its first two years. Difficulties had been cleared away, much progress made and the outlook was all that could be desired. It was added: "To guard against future abuses and to rectify those existing in the preparation and sale of medicine, to extend our knowledge of pharmacy and to improve the science, may be considered the prominent objects of the institution." These, indeed, were never lost sight of. The school had been established and now a library was a pressing need. There was a further review of the care exercised governing the question of conferring degrees, it being determined that this privilege should only follow the most faithful and efficient study. The duty of continuing to guard the public against the imposition and peril of impure and fraudulent drugs was emphasized anew.

In the report for 1823 it was stated that there were upwards of one hundred books in the library. In view of our present great library, covering all departments of pharmaceutical study, this statement sounds pathetic. In this report, first mention is made of the imperative need of a cabinet of specimens. The founders looked abroad for knowledge. At a meeting in September, 1823, a translation of the proceedings of the Society of Pharmacy of Paris was read to attentive listeners; also a translation of an article in the "Journal de Pharmacie," on the best method of preparing a certain syrup. A committee was appointed to continue this enlightening work. At a meeting in November of the same year, a loan of $1000 was authorized towards the library and a cabinet of specimens. This was a bold step, confidently taken. This loan was carried for a number of years and there was great rejoicing when it was paid off. There were no multi-millionaires in those days, to hand around vast sums for public entertainment and enlightenment.

At a meeting in October, 1824, an important step was taken in asserting and maintaining the dignity and honor of the profession of pharmacy and of the dealers in medicine. This was the adoption of a resolution referring to a growing demoralizing custom

of secret partnership between physicians and druggists. It was vigorously declared: "The Philadelphia College of Pharmacy views all such combinations as disreputable and unfair and it recommends to its members to abstain from them and to discourage them as far as possible." A copy of this resolution was sent to the Philadelphia College of Physicians and to the Philadelphia Medical Society, both of which organizations heartily endorsed the declarations made. The College of Physicians asked co-operation in a movement to prevent druggists from compounding medicine for customers without a physician's prescription, and the College of Pharmacy promptly acceded to this timely request.

In March, 1825, the "Journal of American Pharmacy" was conceived and the first number issued a year later. At the last meeting in December, 1828, it was decided to present a gold medal to the student presenting the best thesis for graduation, the subject to be "a full and original analysis in vegetable chemistry."

A Committee Report submitted April 27, 1829, said: "The Philadelphia College of Pharmacy has now been in existence for more than eight years. During that period it has, with slender funds and through many discouragements, effected more for the improvement of American Pharmacy than all that has before been done or attempted in this country. It has produced union and concert, a more liberal spirit and more elevated views among the apothecaries of Philadelphia. It has had the honor of establishing the first school of Pharmacy, which this country has seen. It has established the first and only American journal devoted exclusively to the science and art of the profession. It has resolved a company of shopkeepers into a scientific association. It has educated young men with more accurate science and more extensive knowledge than their predecessors." At this time also, it was decided to take another step forward, through the creation of a loan of $1000 for the purpose of purchasing the most approved chemical and philosophical apparatus for the use of lecturers of the College. The publication committee found itself facing serious problems from time to time. Reference is pathetically made to the "awful chasm" consequent upon delinquent subscribers and those withdrawing subscriptions to the "Journal of Pharmacy," yet they courageously go forward, confident in the belief of renewed support. It was slow work, educating the trade and profession to support periodical publications.

At the beginning of 1831, there were only about forty-five students assured for all the lecture courses. But the College authorities felt encouraged in the belief that its work was destined to widely extend, as its character became more favorably known.

In 1838 the graduating class numbered only nine, and this, seventeen years from the beginning. The curriculum could not be compared with that of to-day, yet it was a severe test for those days.

In 1838 Thomas P. James was elected a member of the college. Twenty-seven years later this gentleman's drug house, No. 630 Market Street, was bought out by my father's firm, French, Richards & Co., after the destruction of their establishment at Tenth and Market Streets by fire.

The first Minute Book covers the years 1821 to 1841, inclusive. The second Minute Book, beginning 1842 and running to 1870, contains a most interesting tabulated statement relating to the officers of the College, over which we might absorbingly linger. It is a record of noble, earnest, unselfish service on the part of men worthy of lasting honor. The names of twenty-eight subscribers to the first building fund, the old hall in Zane Street, are given, that of Dr. Geo. B. Wood near the top, for $800.00. Here are the names of five presidents, from 1821 to 1885, who served an average of thirteen years each; Daniel B. Smith served twenty-five years and Dillwyn Parish sixteen years, he having filled the more laborious office of secretary for twelve years previously. Many other officers served long terms; Charles Ellis was secretary fourteen years and president fifteen years. Henry Troth served in the vice-presidency thirteen years, mostly occupying the chair at stated meetings. To the fidelity, energy and wisdom of these officers of the first half century of its existence, the Philadelphia College of Pharmacy owes an immense debt of gratitude.

At a special meeting in November, 1847, a memorial to Congress was adopted, directing attention to the importation of impure and adulterated drugs and asking the enactment of efficient legislation to prevent a continuance of this growing evil. This suggestion was complied with.

March 31, 1848, the first Code of Ethics was adopted, the College asking its endorsement by the College of Physicians and other medical bodies. This was an important advanced step taken and the effects have been far-reaching and lasting.

The graduates of 1851 numbered 19; those of 1854 reached 26; those of 1856 numbered 28, with 112 students enrolled. The College was steadily marching onward and upward. The graduates of 1869 numbered 48; those of 1870, 51; and for many years past the roll has numbered considerably over a hundred.

At a special meeting December 10, 1867, the first steps were taken to purchase the present site of the College buildings, and in the autumn of the following year, the institution was removed to its present location, Tenth Street below Race. At the forty-seventh annual meeting, March 30, 1868, the following quaint "farewell minute" was read and adopted:

"The members of the College are reminded that the present is the last meeting of the College within the walls of the present building, where, for many years they have so pleasantly conferred together. On separating, and bidding adieux to the present locality, they hope that their next regular assembling will be under pleasant auspices in a building much better adapted to the growing necessities of the College, and that each member will feel a renewed interest in the Philadelphia College of Pharmacy."

Renewed interest *was* awakened; and during the forty odd years the College has continued to occupy its present home it has unceasingly grown, and strengthened, and developed in every direction until it stands to-day, as it justly merits, at the head of all institutions of the kind in the world.

In the ninety years of its existence about 20,000 students have been instructed; some of these are widely known as the brightest and most successful professional and business men of the time, measuring up to a very high standard of learning and efficiency. And it is of more than ordinary interest to note, that it is a rare exception to find a large pharmaceutical establishment in the United States that is not directly or indirectly under the management of a graduate or former student of the Philadelphia College of Pharmacy.

With a commanding college home furnished with all scientific paraphernalia of the most modern type; splendidly equipped departments of research and experiment; advanced courses of instruction that would have appalled the early graduate; a corps of

instructors thoroughly competent, enthusiastic and zealous in the performance of their special duties, in every way equal to the most exacting demands of the times—our College occupies a foremost position in the line of scientific discovery and practical utilization of new ideas according to the most approved methods. It is a self-confident leader, not a timid follower.

Having a just pride in the past which has a record rich in usefulness and honor, it behooves us to push on to still higher and greater things that the achievements of the future may meet our highest and worthiest expectations.

PHILADELPHIA COLLEGE OF PHARMACY.

NINETIETH ANNIVERSARY.

Some weeks ago the president of the Philadelphia College of Pharmacy sent the following invitation to the officers, members of the Board of Trustees and faculty, the Mayor of Philadelphia and the heads of our sister institutions:

Mr. Howard B. French
requests the pleasure of
.........................'s
Company at Dinner
Thursday evening, February 23, 1911,
at seven o'clock,
Union League Club,
In celebration of the Ninetieth Anniversary
of the founding of the
Philadelphia College of Pharmacy
at
Carpenters' Hall.

While the members of the college recognize the significance that must necessarily be attached to the attainment of the centenary of the founding of the oldest college of pharmacy in this country, as shown by the appointment of a committee even at this early date to devise and consider plans for the celebration of its one hundredth anniversary in 1921, it is probable that the members for the most part had not considered the desirability of observing its ninetieth anniversary, and hence this invitation from President French must have come as more or less of a surprise.

It showed, however, how closely he is in touch with the progress of events and how much he has at heart the work of the college. The dinner was held in the celebrated banquet hall of the Union League, where all of the official dinners in honor of great events or the achievements of distinguished men were formerly held. On the historic oval table around which the diners gathered was a magnificent display of flowers, including freesia, narcissus, antirrhinum, and lilacs with a background and setting of *Smilax laurifolia* and fronds of the Boston fern. The menu, which was well selected, was served in accordance with the service of this famous club.

The printed menu was in the form of a booklet, which contained a list of the names of the officers, faculty and instructors of the college and of the invited guests, and was bound in Morocco leather with an imprint of the seal of the college and two illustrations, the one showing Carpenters' Hall where the college was organized in 1821 and the other, the present college building. On the last page inside the cover were the words, " Organized, 1821, P.C.P. Progressing 1911."

At the conclusion of the dinner the host, President French, read an interesting historical sketch of the college, which is published in another part of this issue of this Journal. He then called upon Hon. John E. Reyburn, Mayor of Philadelphia, who delivered a most earnest address on the relationship of the institutions of learning to the city. He was generously applauded for his remarks, in which he said that he hoped that it would be possible to bring all of the educational institutions of Philadelphia together at a common centre on the new Parkway Boulevard. He further stated that his idea was not that they be absorbed or lose any of their individual character, but that they might derive all of the benefits of close association and neighborly contact. Hon. Henry F. Walton, President of the Medico-Chirurgical College, was the next speaker, and he heartily endorsed all that the Mayor had said in regard to the importance of the close association of independent schools and then remarked that he was pleased to bring the felicitation of the Medico-Chirurgical College to the officers and faculty of the Philadelphia College of Pharmacy gathered on this eventful occasion.

Dr. J. W. Holland, dean of Jefferson Medical College, said that he brought the warmest congratulations of the " twin-sister " of the Philadelphia College of Pharmacy. He stated that while Jefferson was founded four years later than the Philadelphia College of

Pharmacy, her first graduating class was sent forth in 1826, which was the time of the graduation of the first class of the Philadelphia College of Pharmacy. He also referred to the fact that while a number of students of the Philadelphia College of Pharmacy had gone to Jefferson Medical College, this college also gave to the medical faculty of Jefferson, Professor Franklin Bache, who was connected with the faculty of Jefferson Medical College for seventeen years. Brief addresses were also made by Vice-President Jos. L. Lemberger, and Professors Remington, Sadtler, Kraemer and Moerk.

The addresses of the Mayor and some of the other speakers not only hinted at the general scheme for the improvement of Philadelphia, which has been worked out by experts in their respective lines, but showed that the scheme comprehends a more or less definite plan for the improvement and, to some extent, co-ordination, of the educational institutions of the city. In addition, a fresh impetus was given the active workers of the college by the opportunity afforded to commingle at the same board and by reason of the rehearsal of the ideals and deeds of those who had gone before, to press forward to the century mark with renewed zeal and earnestness. The occasion was one which was encouraging to the older men who had been actively engaged in the work for these many years, and likewise an inspiration to the younger men upon whom the responsibilities of the future rest.

H. K.

NOTES AND NEWS.

A PORTRAIT OF PRESIDENT FRENCH will be presented to the College at a testimonial dinner to be given at the Union League, on Tuesday, April 4, 1911, at seven o'clock. This promises to be one of the most interesting occasions in connection with recent affairs of the college.

A HANDY REFERENCE BOOK. The *Druggists' Circular* has recently published the second revised and enlarged edition of their book on "The Modern Materia Medica." This work contains much valuable information regarding the description, tests, therapeutic action and doses of all of the newer substances that are likely to be prescribed, and will be found of very great assistance to the practical druggist who is expected to know something of these things at a moment's notice.

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APRIL, 1911

A REVIEW OF THE CHEMICAL WORK DONE ON THE ACTIVE PRINCIPLE OF ERGOT.

By Alfred C. Crawford,
Pharmacological Laboratory, Leland Stanford, Junior, University.

Biological tests have shown that different ergots vary much in their activity; some are apparently devoid of any medicinal or poisonous action. This inactivity has not yet been proved to be associated with definite macroscopic peculiarities of ergot, or with peculiarities of the host upon which it grows. Ergot grown on rye is what is officinally referred to under the term ergot.

The biological method of testing ergot has been much discussed in recent years. For a long time the majority of investigators rested content in the belief that the principle which produced the bluing of the cock's comb was the one to which the therapeutic action of ergot was due, and that on this basis the drug could, at least approximately, be standardized for clinical usage. Later investigations tended to discredit this view, suggesting that the principle or principles which induce uterine contractions may not necessarily be those which cause bluing of the cock's comb, and that the latter may have a subordinate rôle in medicine.

Owing to the peculiar chemical difficulties inherent to this subject, our knowledge of the active principles of ergot has been based largely on so-called pharmacological isolations, which have not answered strict chemical requirements. To form any accurate idea as to the methods for the standardization of ergot it is necessary to know something of the historical development of the

work done on the isolation of the active principles. Unfortunately various investigators have used the same name for different preparations, and have used different biological tests as their guide in determining the activity of such preparations, so that, for clearness it is necessary to discuss in some detail the work of each, although the names of these workers are now unimportant.

Ergot has been used by the Chinese as an oxytocic for over one thousand years, but there are only a few records of its use in modern medicine until Stearn's article [1] (1807) appeared. The earlier workers were engaged in proving the relation of ergot to the various complex-of-symptoms which have received the name "ergotism." [2] Salerne [3] (1754) and Tessier (1778) found that gangrene occurred in young pigs after the administration of ergot, while Dietz (1830) noted that one to three ounces of ergot would cause gangrene of the comb and wings of birds. From an early date ergot was believed to possess a specific action upon the uterus and the small arteries.

The recorded chemical work on ergot dates back to 1717, but the reports of the early investigators, such as Tessier,[4] Mass, Pettenkofer (1817), and others need only be referred to. In 1817 Vauquelin and in 1831 Wiggers [5] called attention to the large amount of oil in ergot. Wiggers denied the presence of hydrocyanic acid in it. This acid had been obtained by Pettenkofer by burning ergot with caustic potash, but Roberts believed he had obtained a reaction for it in an aqueous extract. Wiggers recognized a sugar which Liebig and Pelouze claimed to be mannit, while others believed it to be mucose.[6] This mucose has been found to be trehalose.[7] Later both mucose and mannit were claimed to be present in ergot.

Wiggers removed oils, etc., from ergot by means of ether and extracted the residue with alcohol. The portion of this extract which was insoluble in water he called ergotin. This must necessarily represent a mixture and not a chemical individual. He fed 9 grains of this ergotin to a cock and induced convulsions and death. This amount corresponded to about one and one-half ounces of ergot. He noted that the comb became cold, but said nothing as to its bluing, and inferred that ergotin represented the toxic principle, while the aqueous extract represented the therapeutically active agent, the active principle was believed to reside in the aqueous extract and was probably due to a so-called "ozmazom."

Dietz found that the aqueous extract of ergot possessed the same action as ergot itself, while Schroff [8] claimed, that in man, Wiggers' ergotin produced the essential symptoms seen after ergot administration. Wiggers also obtained a wax-like body which he called cerin.

In 1840 Wright,[9] from clinical observations and also from experiments on dogs and birds, claimed that the oil obtained from ergot contained the active principle. This oil was extracted from ergot by means of ether. Sir J. Y. Simpson in speaking of this oil said, "I have repeatedly employed your preparation of the ergot, and have always preferred it of late, because it has appeared to me to act with more precision than the infusion of the powder, and its dose is more easily regulated. I have used it both in cases of lingering parturition, dependent on deficient uterine contractions, and also in instances of post-partum hemorrhage." Wright imagined that the oily body obtained by distilling dry ergot, and that obtained by treating ergot with liquor potassæ, was the same as the one which may be obtained by extraction with ether. Perhaps the differences may explain certain variations in the reports as to the action of this oil. No doubt in these extractions of oil various compounds were contained.

The name ergotin was also used by Bonjean [10] (1842) for an aqueous extract freed from some extraneous matter by precipitation with alcohol. It was not claimed to be a definite chemical, but rather a pharmaceutical preparation. The ergotin of Bonjean was also called "Extractum hæmostaticum," as he believed it to be an efficient agent for controlling hemorrhage. Bonjean denied that Wiggers' ergotin was active. He noted that after the administration of ergot, animals developed a "narcotic" condition, which he compared to that resulting from the administration of morphine, and called attention to the fact that the combs and wattles of cocks turned blue. Bonjean said the principal therapeutic agent was the aqueous extract, but that the poison was an oil, soluble in ether. This oil lost its poisonous property by being boiled. Kohler,[11] by experiments on frogs, showed a difference in activity between the ergotin of Wiggers and Bonjean's preparation. Schroff noted that 1 gm. of Bonjean's ergotin caused abortion in a rabbit.

Hooker [12] (1852) found that the oil extracted by ether slowed markedly the pulse rate in a young man. This slowing of the

heart by ergot and its preparations was also called attention to by a number of workers. Hooker inferred that the capillary circulation was disturbed, because " a portion of the skin deprived of its blood, by pressure with the finger, being a long time in recovering its color " and noted that there was also an increased secretion of urine. According to him, the ethereal extract possessed no ecbolic action, but the residue after the extraction still exerted this action.

Parola[13] claimed that the oil obtained from ergot was inactive and that the activity of ergot was to be traced to a resin extracted with the oil. However, the term resin is apt to be a vague one. Betrand,[14] by experiments on himself and on animals, corroborated Parola's statements as to the inactivity of the oil. Arnal[15] (1848) claimed that neither the ethereal nor the aqueous extract contained the real toxic principle, but that it resided in the residue after such extractions. He believed the hemostatic action of ergot to reside in the aqueous extract and to be associated with the depressant action on the heart, and claimed that the irritation of the intestines was an important feature of the action of ergot. He also noted that the aqueous extract acted as a diuretic. During one day eight grams of ergot were given to a cock; and on about the seventh day, the bird became dull. In some cocks similarly fed, the comb turned blue; in others, there were ulcerations of the comb with emaciation and death.

Herrmann made the interesting observation that the evaporated ether—extract of ergot, on treatment with alkalies, developed the odor of ammonia and of trimethylamin.

Winckler[16] in 1827 recognized a volatile base which he called secalin (propylamin), and believed that the ergotin of Wiggers was a combination of resin with propylamin. This propylamin[17] was later found to be trimethylamin, although at one time it was believed to be methylamin.[18] Gerres,[19] in 1862, unfamiliar with Winckler's work, also reported the presence of a volatile base which he named secalin and noted that an aqueous extract when shaken with sodium bicarbonate and ether imparted the odor of ergot to the ether. He also observed that on evaporating a tartaric-acid-alcohol extract of ergot and shaking the evaporated mass with sodium bicarbonate and ether it yielded a residue which produced in a rabbit acceleration in the pulse-rate and trembling.

In 1864[20] Wenzell described a volatile acid, which he named ergotic acid, and also two amorphous bases which he described as

alkaloids. He precipitated an aqueous extract of ergot with lead subacetate to remove impurities and then precipitated the filtrate by means of mercuric chloride and bicarbonate of potassium. After decomposing this precipitate with H_2S, the two bases were separated by means of mercuric chloride. As its name would imply, he believed the first base to be the medicinally active agent, however, no analyses were made of these compounds. This view that ecbolin was the active agent in ergot was based on its supposed action on the spinal cord of man, which action manifested itself by involuntarily muscular contractions, etc. The activity of ecbolin was also inferred from one experiment in controlling uterine hemorrhage. Wenzell later separated his bases by means of the insolubility of ecbolin in ether. On warming an extract with caustic potash an odor of propylamine, in reality trimethylamine, was obtained. This work was corroborated by Herrmann [21] as to the presence of ecbolin, the only one of Wenzell's bodies he searched for, and by Ganser [22] as to the presence of ecbolin, ergotin and ergotic acid, while Manassewitz [23] found ergotin only present and with it a formate. As in Wenzell's experiments, the precipitates which Manassewitz obtained with mercuric chloride yielded trimethylamine on treatment with caustic potash. Haudelin,[24] by experiments on cats, failed to corroborate Wenzell's work. He found that both the precipitate and filtrate with mercuric chloride and sodium carbonate were inactive to cats on intravenous injection. He noted that the active principle was insoluble in alcohol and could not be precipitated with lead subacetate and ammonia. Dragendorff and Podwissotsky found both ecbolin and ergotin inactive to frogs. Rossbach claimed that there were only quantitative differences between Wiggers' ergotin and Wenzell's ecbolin. Wenzell noted that the reaction of an aqueous extract of ergot was acid, and believed this due to the presence of acid phosphate of magnesia.

Blumberg [25] thought there was only one alkaloid present in ergot and that ergotin and ecbolin were identical. The filtrate from which Wenzell obtained his ergotin was found by Blumberg to yield trimethylamin, while the precipitate which should contain ecbolin yielded none.

According to Kobert, the compound which excites uterine action has nothing to do with the substance which forms the main mass of Bonjean's extract and of Wenzell's dialyzed ergotin.

Wernich [26] traced the action of ergot to the water-soluble

sclerotic acid. He used the contraction of the blood vessels of the frog as his guide and found that the ether extract of ergot caused no contraction of these vessels. His preparation was placed on the market as "dialyzed ergotin," the dialysis being used to free it from certain extraneous matter. Wernich reported that, after ergotin administration, the bladders in numerous cases were found distended, owing to an increased secretion of urine. This observation agrees with that of Hooker already mentioned. Kokorin is reported to have noted that, after injecting Wernich's preparation, dry gangrene occurred at the site of injection.

Buchheim [27] (1874) failed to obtain any active principle, and traced the acidity of ergot to lactic acid and its activity to decomposition products of proteins. His most important work was to prove the presence of leucin, which he showed yielded amylamin on heating in a test tube.

Dragendorff and Podwissotsky [28] called attention to the presence in ergot of 0.4–1.15 per cent. phosphoric acid, and strange to say, the activity of ergot was traced by Leri to this acid. Its presence was originally noted by Vauquelin. Dragendorff and Podwissotsky somewhat purified sclerotic acid and named it sclerotinic acid and traced most of the activity of ergot to it, but some of the activity was attributed to a colloid body which they named scleromucin. They also noted the presence of a base, picrosclerotin, yet they did not attribute the action of ergot to it. Their tests were made on frogs and seem unsatisfactory. From experiments on pregnant and non-pregnant animals and also on the isolated uterus, Kobert claimed that sclerotinic acid did not excite uterine contractions, and Ganguillet [29] and Rennert [30] pronounced it worthless for clinical purposes. The clinical experiments of Fehling and v. Scanzoni also indicated that sclerotinic acid possessed no marked therapeutic activity to excite uterine contraction. Dragendorff and Podwissotsky also claimed to have proved the presence of various coloring matters, sclererythrin, sclerojodin and scleroxanthin together with a crystalline body sclerokrystallin. Podwissotsky noted that on treating sclerotinic acid with alkalies it lost its activity and ammonia developed. The view that the activity of ergot was mainly due to sclerotinic acid was corroborated by Nikitin's work.[31]

Zweifel [32] also traced the activity of ergot to a water-soluble acid principle, and based his conclusions on the action of this

preparation on the blood vessels of the frog. He found that sclerotinic acid excited uterine contractions in pregnant animals without injury to the fœtus and that it also induced peristaltic movements of the intestines and caused contraction of the blood vessels. This action on the intestines had been previously noted by Bonjean.

As it was still a question as to which of these principles were responsible for the action of ergot, Denzel,[33] believing the uterine action of ergot to be due to all the above constituents, made his preparation so as to contain both the bases and the water-soluble principle. Mauk [34] found this preparation to be efficient in many cases of labor, but Scanzoni and Bumm, on account of severe symptoms which followed its use, reported it unsuited for clinical usage.

The most important of the earlier chemical work was done by Tanret,[35] who reported the presence in ergot of an alkaloid, which he named ergotinine. This was probably identical with the picrosclerotine of Dragendorff and Podwissotsky. Tanret believed that ergotinine existed both in a crystalline and in an amorphous condition, with a preponderance of the amorphous variety. In old ergot the crystalline form especially diminished, thus one kilogram of fresh ergot yielded 1.2 gm. alkaloid, of which one-third was in the crystalline form, but after two years' preservation, a specimen of ergot gave 0.4 gm. only of alkaloid, one-fifth of which was crystalline ergotinine. He considered the amorphous alkaloid merely a molecular modification of the crystalline form. This latter increased the solubility in alcohol of the crystalline variety. He obtained ergotinine by extracting crude ergot with boiling alcohol and then making the alcohol alkaline, and after evaporation, shaking the residue with ether. On the addition of a citric-acid solution the alkaloid separated from the ethereal solution and was afterward purified. It gave an odor of methylamine when treated with strong caustic hydrate. On treating ergotinine with concentrated H_2SO_4, in the presence of a little alcohol, this alkaloid gave a yellowish-red color which passed into a blue. Ergotinine solutions showed a peculiar fluorescence which was compared with that of quinine. Ergotinine was sold under the name ergotininum citricum solutum. Besides ergotinine, Tanret also claimed the presence of a cholesterine-like body, ergosterin, a base containing sulphur ergothioneine, and a volatile alkaloid. A volatile coniine-like base had been previously noted by Winckler. The ergosterine of Tanret is probably the same as Wiggers' waxy-like cerin and the cholesterin of Ludwig.[36]

In 1886 Kobert[37] reported a crystalline specimen of ergotinine to be inactive on the uterus and that it also failed to produce bluing of the cock's comb, although he had in 1883 stated that ergotinine (Tanret) would cause marked toxic action in frogs and a rise in blood pressure in rabbits. Meulenhoff reported ergotinine inactive, however, Blumberg found that 20 mg. would kill frogs, while in Palm's hands 0.01 gm. caused little or no bluing of the cock's comb. The clinical reports of its use also varied.[38]

Galippe and Budin[39] noted no symptoms in a dog after the subcutaneous injection of 30 mg. of Tanret's ergotinine, but 80 mg. induced colic and vomiting with a lowering of the temperature, while a syrup containing 105 mg. of ergotinine induced death. One milligram of this ergotinine represented 1 gm. of ergot. Dujardin-Beaumetz noted similar nausea and vomiting to occur in man after the injection of 4–5 mg. of this alkaloid. In one case puerperal hemorrhage was apparently arrested by it, yet the arrest only occurred after hours of delay and there must necessarily be an element of uncertainty in this case. Others reported favorable clinical action from its use.[40] The confusion in the reports is probably due to the fact that some of the specimens used were wholly crystalline, while others were a mixture of the crystalline and amorphous varieties.

In 1884 Kobert[41] announced the presence of three bodies in ergot —a base, cornutin, and two with acid properties, ergotinic acid and sphacelenic acid. Kobert isolated no body chemically pure. His isolations were merely physiological. The term ergotinic acid had already been used by Merck for Zweifel's preparation.

Ergotinic acid subcutaneously injected, acted as a paralyzant on the brain and spinal cord, but caused no bluing of the cock's comb, and was inactive on the pregnant uterus of sheep, cats, rabbits, and dogs. By mouth it was inactive, either being unabsorbed or destroyed in the gastro-intestinal tract. Sphacelenic acid received its name from the old name of ergot, Sphacelia segetum. Kobert believed the specific action of ergot was due to this resinous acid,[42] although he admitted that he had not isolated it in a chemically pure condition. Sphacelinic acid caused bluing of the cock's comb and had the characteristic action on the uterus. Kobert introduced the cock's-comb test as a guide for the recognition of this acid. Cornutin, except in toxic doses,[43] produced no uterine contractions and caused no bluing of the cock's comb, but

in frogs even 1/32 mg. induced convulsions. However, Meulenhoff failed to note these convulsions. Kobert[44] said distinctly that his cornutin was different from the crystalline or amorphous ergotinine of Tanret and that there was no resemblance physiologically. The ecbolin of Wenzell was probably the same as Kobert's cornutin.

Later, Kobert modified his original view[45] and stated that cornutin would produce uterine movements in pregnant and non-pregnant uteri, but in non-pregnant animals the dose must be large. Sphacelenic acid produced uterine contractions, tetanic in character and associated with toxic symptoms, while cornutin induced normal intermittent ones. According to Kobert cornutin acted on the spinal centre, while sphacelenic acid acted directly on the uterus. Cornutin produced marked narrowing of the arteries of uterus. The therapeutic action of ergot was believed by Kobert to be a resultant of the action of both compounds. Palm showed that even 0.005 gm. of cornutin would produce bluing of the cock's comb with dyspnœa. This preparation[46] freed from ergotinic acid was then introduced on the market and used clinically,[47] as a hemostatic or oxytocic, generally with success. The work of Kobert was confirmed by Grünfeld so far as sphacelenic acid was concerned and by Lentaker as to cornutin.[48] In Ludwig and Savor's experiments the cornutin preparation of Kobert failed to produce the full characteristic action in cocks, when given in doses corresponding to the proper amount of ergot, and with them clinically the results were disappointing.[49] Cornutin (Kobert) has been tested physiologically by Lewitski. He found that 1.5 to 2 mg. per kilo of this preparation caused abortion in animals in the later stages of pregnancy. He also reported favorable clinical use without toxic symptoms. Kobert's views were mainly upheld by his pupils. According to him, no ergot retained its therapeutic powers over twelve months.

Kobert's change of view would suggest that he was dealing with a chemically impure body. Tanret considered Kobert's cornutin a partially altered ergotinine.[50] Kobert finally summed up his work by saying that there was an inactive and an active modification of the ergot alkaloid; the active one he believed was cornutin and the inactive one was the crystalline ergotinin of Tanret.[51]

Keller's[52] work was based on the idea that an alkaloid is the active principle of ergot and on this basis he devised a method

of separating the alkaloid or alkaloidal mixture. It is based on the experiments of Kobert, which showed that the alkaloid was soluble in ether, and on Wenzel's observation that it was insoluble in petroleum ether. This more or less pure body Keller has named cornutin, on the basis that his preparation is the same as Kobert's cornutin. The adoption of this name has given rise to much confusion. Wyss tested Keller's cornutin and claimed that it agreed in action with that of Kobert, but the nature of the test is not stated; presumably, it was the bluing of the cock's comb. Keller at first believed his cornutin was identical with the ergotinine of Tanret and the cornutin of Kobert, while the picrosclerotin of Dragendorff and Podwissotsky was considered to be the same compound admixed with certain decomposition products. He called attention to the fact that cornutin could be precipitated from an ethereal solution by petroleum ether. In addition to the color noted by Tanret, a sulphuric acid solution of the alkaloid, on the addition of $FeCl_3$ or other oxydizing agents as bromine water, gave an orange red which passed into a blue and then bluish green. To secure the best results the alkaloid is first dissolved in acetic acid and sulphuric acid is then added.

Later Keller adopted the view of Tanret, that Kobert's cornutin was a decomposition product of ergotinine, and showed that his cornutin, if treated with acid, yielded a body having the character of Kobert's cornutin.[53] He has proposed a method which has been used by various firms[54] for quantitative determination of the active principle. Keller's method is as follows: Twenty-five grams of dried ergot are extracted with petroleum ether until the extract gives no residue. After drying with moderate heat it is transferred to a weighed vessel of about 250 c.c. capacity, and 100 grams of ether are poured over it; after about ten minutes, milk of magnesia, made by shaking one gram of calcined magnesia with 20 c.c. of water, is added and the mixture is shaken thoroughly. After half an hour 80 grams of the ethereal solution are poured off. Four grams of the ether solution correspond to one gram of ergot. If the solution is not clear, it is allowed to stand, and then shaken three times with dilute HCl (0.5 per cent.), using 25, 15 and 10 c.c. If necessary it is shaken a fourth time with 10 c.c. of the same and the last shaking is tested with Mayer's solution to see if the extraction is complete. The acid solution is then shaken with ether and ammonia, and the shaking repeated twice,

then filtered and distilled in a weighed vessel. After treating with ether and exaporating, the residue is weighed. The cornutin content of six samples of ergot varied from 0.095 to 0.225 per cent. According to Dohme, German ergot as occurring on the American market assays at 0.15 per cent., Spanish ergot at 0.29 per cent., and Russian ergot at 0.18 per cent.

On frogs (R. Esculenta), Santesson[55] tested this cornutin in doses of 1–20 mg., and as no convulsions were produced, inferred that it was therefore different from the cornutin of Kobert, but Palm[56] has shown that 0.005 gm. of cornutin obtained from certain ergots by Kobert's method failed to produce convulsions in frogs. Meulenhoff reported a similar experience. Evidently the convulsive action of Kobert's body must be due to some accidentally present body which may not necessarily be present in all ergot preparations. Santesson claimed that in pregnant rabbits Keller's cornutin failed to produce any uterine action save in toxic doses. Santesson's failure to produce a rise in blood pressure in rodents with cornutin does not argue against the presence of a blood-pressure-raising principle, as rodents are especially insensitive to this action. Santesson, by injecting 5 mg. intravenously into cocks, produced a rise in blood pressure, while 15–25 mg. injected hypodermically into these animals produced a marked discoloration of the comb.

One of the objections urged by Santesson against Keller's work, is that Keller's analysis of an ergot preserved for two years, showed a relatively large percentage of cornutin. Ergots long preserved are considered inactive, but the clinical work of Bischofberger indicated that two and three year old ergot still caused uterine contractions;[57] however, one must be careful in interpreting clinical experiments. Unfortunately Keller failed to control his analysis with physiological tests. Tanret a few years previous had pointed out that although the alkaloidal content of old ergot diminished, it was mainly the crystalline alkaloid which was lessened. The truth of the matter probably is that by Keller's method more than one alkaloid is extracted—a view which Keller later adopted.[58] Keller made no analysis of his cornutin—of itself a suggestion that he was not sure of its chemical purity.

Several years ago the writer examined[59] the products obtained during the various stages of the Keller-assay method and found in the alkaline-ether-"shaking" apparently all the principles which

caused bluing of the cock's comb, while the residue was inactive in this respect. At times it seemed as if the ether-shaking was more active than the original fluid extract which was used. This extract would induce a marked rise in blood pressure in dogs with cut vagi. It must be remembered that besides the alkaloids other bodies, such as basic amines, which might contribute to its pressor activity, go into this ether. As there is probably more than one body in this shaking it seems at present unsafe to trust this method alone. However, Keller's method is a safe one for determining the amount of bases present, or at least the ether-soluble bases.

Schaerges [60] states that Keller's cornutin is not present in ergot as such, but as ergotinine. Barger and Dale believe this cornutin to be a mixture of ergotinine with 25 per cent. ergotoxine. Keller's preparation is on the Swiss market under the name "Secornin."

The next important step was undertaken by Jacobj.[61] He first removed from ergot, by means of petroleum ether as much of the oil [62] as possible, and then extracted the active principle with ether. After this extraction the ergot caused no bluing of the cock's comb. The ether was precipitated by means of petroleum ether and the precipitate was redissolved in ether and afterwards fractionally precipitated by petroleum ether. When dissolved in sodium hydrate, 0.1 gm. of this precipitate, which contained no nitrogen, caused bluing of the cock's comb and did not produce convulsions, while a similar injection of from 0.1–0.2 gm. induced regular normal uterine contractions with abortion in pregnant animals, unassociated with any toxic effects, either to the mother or to the young. In some animals, such as cats, its intravenous injection was followed by a rise in blood pressure, but usually this action was not marked. In these cases the vagi were uncut and the central nervous system was intact. However, if the spinal cord was cut, Jacobj noted a rise after such an injection. The preparation was named chrysotoxin ($C_{21}H_{22}O_9$). This yellowish brown body is soluble in ether, chloroform, benzol, alcohol and caustic alkalies, but insoluble in water and in dilute acids. Under the influence of an excess of alkali it is transformed into ergochrysinic acid which is inactive. However, an active combination of chrysotoxin with sodium can be obtained by precipitating its ethereal solution with an absolute alcoholic solution of sodium hydrate, but in this case an excess of alkali is to be avoided. This combination is known as spasmotin. According to Dale, chrysotoxin contains about 90 per cent. impurities.

If the original ethereal solution is not carefully fractioned with petroleum ether the chrysotoxin is admixed with a nitrogenous body. When such a precipitate is treated with glacial acetic acid a portion only dissolves. The portion which remains undissolved, when taken up in ether, gives a precipitate with petroleum ether. This has a golden yellow color and is inactive on the cock's comb. It has received the name ergochrysin.

On treatment with sodium carbonate, the acid solution of the crude precipitate yielded a gray alkaloidal precipitate which was named secalintoxin ($C_{13}H_{24}N_2O_2$). This is about four times as active as chrysotoxin in producing bluing of the cock's comb and is free from any convulsant action. Secalintoxin has the same action as chrysotoxin, but differs from it in degree. Jacobj says that under certain conditions a marked rise in blood pressure may follow its injection. Secalintoxin is a white powder which is soluble in alcohol, benzol, chloroform, and slightly so in ether. It gives a violet color on evaporation with an alcoholic solution of HCl. An oxalate, a phosphate and other salts were obtained by precipitating its ethereal solution with the corresponding acids. It was noted that on standing, the oxalate separated into two portions, one less soluble than the other, but this did not suggest to Jacobj that they were possibly two oxalates.

When the precipitate of secalintoxin is dissolved in a mixture of ether and alcohol and treated with petroleum ether, a greenish mass is precipitated along with some crystalline needles. Jacobj believed that by this means he had separated the basic portion of secalintoxin, but one would hardly expect such a method to free a base from its combination. These needles have received the name secalin and their formula was determined to be $C_{29}H_{55}N_6O_{14}$. They gave a violet colored reaction with alcoholic HCl. These crystals are presumably the same as Tanret's crystalline base. Jacobj expressed a doubt as to this identity, on the ground that his N. determinations did not agree with those of Tanret, but it has since been shown that Tanret's figures are too high and should be close to those of Jacobj. Even 40 mg. of these crystals failed to produce bluing of the cock's comb, and they were also devoid of convulsant action. The greenish precipitate with which these crystals were mixed, in 0.005–0.008 gm. doses caused bluing of the cock's comb. Jacobj believed this resinous, readily-decomposable body to be the active principle of ergot, and has named it sphacelo-

toxin, because Schmiedeberg had previously used the term for the unknown active constituent of ergot. The combination of ergochrysin with sphacelotoxin was named chrysotoxin and that of secalin with sphacelotoxin was designated secalintoxin. Palm corroborated the activity of Jacobj's preparation by clinical observations and also by animal experiments.

Meulenhoff [63] essentially corroborated Jacobj and stated that the active principle of ergot was sphacelinic acid. This he believed identical with sphacelotoxin but retained Kobert's nomenclature, using the term sphacelinic acid. He claimed the presence of but one alkaloid, ergotinine, which he considered only partly active. Kobert claimed that spasmotin was weaker than his sphacelinic acid and warned against its clinical use, as he believed that it was merely sphacelinic acid and had all its disadvantages.

Rielander [64] has corroborated the work of other investigators in finding both betain and cholin in ergot. By injection he showed that these bodies were not responsible for the local gangrene which appears at the site of an ergot injection. In addition to these compounds he found both tetra- and penta-methylendiamin. As to whether these exist as such in ergot or are products from the reagents is not proven. Ludwig,[65] years before this, claimed that methylamin was present in ergot, while Ganser denied that methylamin, or trimethylamin existed as such in ergot. Tanret traced methylamin to the decomposition of his ergotinine. It is to be presumed that the free ammonia which Vauquelin suspected to be present may be in reality an amine.

Vahlen [66] has recently introduced a crystalline principle, which he obtained by evaporating the aqueous extract of ergot and extracting the residue with hot alcohol (75 per cent.). On cooling this alcohol crystalline needles, which he named clavin, separated. The crystals varied in form when other methods of separation were used. They melt at 262–263° C. and are soluble in water, and their solution reacts neutral to litmus. Clavin is not precipitable by caustic alkalies, by alkaline carbonates or by alkaloidal reagents, and is insoluble in petroleum ether, ether and absolute alcohol. Vahlen was unable to determine accurately the yield of clavin, but stated that one kilogram of ergot yields a few grams of this substance. He has calculated the empirical formula to be $C_{11}H_{22}N_4O_2$, and believes, on the basis of his molecular weight determination, that in aqueous solution it dissociates into two bodies which have approxi-

mately the same molecular weight. Barger and Dale object to this determination in glacial acetic acid and believe Vahlen's formula incorrect.

Vahlen noted that on heating these crystals the reaction resembled that with leucin, an amino-acid which Buchheim had previously found in ergot. According to Vahlen, when 0.194 gram of clavin was injected into the vein of a cock, it produced no bluing of the comb; it is probably devoid of toxicity, as 2.6 grams per kilo injected subcutaneously into mice produce no symptoms save some dulness. According to him, the second constituent could be represented by the formula $C_5H_{11}O_2N$, although its structure is as yet unknown, and he believes that it is the physiologically active constituent of clavin. This is claimed on the basis that, as clavin is active and leucin is inactive, the second constituent must be the active one.

Van Slyke has noted that the "properties of clavin are almost identical with those of the isomorphous mixture of leucin and valin." The main difference is in its melting point. He corroborates Barger and Dale in proving the presence of leucin in clavin, but indicates the presence of valin, which these investigators had at first overlooked. Van Slyke [67] suggests that a mixture of leucin and valin should be tested physiologically. Shortly after Van Slyke's paper appeared, Barger and Dale reported the presence of valin in clavin along with asparaginic acid. It is interesting to note that Barger admits that some of the activity in ergot is due to iso-amylamin which may be derived from leucin.

The evidence at present is against clavin being the active principle of ergot. Barger and Dale suspect that the activity of clavin is due to some admixed p. oxyphenylethylamin.

Kraft [68] has studied the ergot question and has proved that the bodies described by Kobert and also those of Jacobj are not chemical individuals. He isolated two bases which he considered to be alkaloids. One of these is identical with the crystalline base of Tanret, so that Kraft retained the name of ergotinin which Tanret had originally used. According to Kraft its empirical formula is $C_{35}H_{39}O_5N_5$. The second base received the name hydro-ergotinin, as it was considered to be a hydrated form of ergotinin, therefore its formula would be $C_{35}H_{41}N_5O_6$. These alkaloids were obtained from an ethereal extract by shaking it with a tartaric-acid solution, then freeing the bases with soda, again shaking

into ether and crystallizing from methyl alcohol. The two alkaloids were separated from one another by means of their sulphates. Apparently these bases could be transformed one into the other. Kraft also determined the presence of several lacton acids, secalonic acid and certain of its derivatives. As to whether these products are related to the crude scleroxantine of Dragendorff and Podwissotski is not considered. Kraft also found an oil, betain, cholin, mannit which had been noted by previous workers, Tanret's ergosterine and tri-methylamin which he believed were derived from betain. Walz had called attention to tri-methylamin in ergot, and Brieger [69] in 1887 believed it traceable to cholin or isocholin. Kraft first used Keller's method of extracting the bases from ergot by means of alkaline ether, using MgO to secure alkalinity and to free them, but found that he could obtain these bodies by means of ether without adding the alkali and, therefore, argued that the alkaloids existed in a free condition, a suggestion which had been previously made by Keller.

The physiological testing of these preparations was done by Jacquet. He tested the precipitate obtained from an ethereal extract by means of petroleum ether. This precipitate would correspond to Jacobj's chrysotoxin. When administered as a powder, or an oily emulsion, to cocks it caused no bluing of the comb, but if dissolved with NaOH, the filtrate, on injection into cocks, produced a bluing of the comb, and a similar injection into pregnant rabbits was followed by abortion. To produce this action in guinea pigs 0.25 gm. of the crude substance was required. This would really represent 50 gm. of ergot.

After dissolving in glacial acetic acid and diluting with water, 0.02 gram of ergotinin was injected into a pregnant guinea pig. This animal died in twenty-four hours with symptoms of ascending paralysis. There was no abortion.

After dissolving in the same acid and lessening the acidity with NaOH, 0.013 gm. of hydroergotinine was injected into a cock. This injection was followed by a typical bluing of the comb, but the animal died the next day. A similar injection of 0.01 gram of hydroergotinine caused bluing of the comb, but the animal did not die. An injection of the same amount of this base into a pregnant guinea pig caused convulsions. After two days 0.025 gm. more was injected into this animal. Twitchings of the muscles and restlessness were observed and four days later immature young were

born. The injection of 0.04 gram of the hydroergotinine was made into a pregnant rabbit and two days later 0.05 gm. more given. On the third day this animal died of inflammation of the lungs and had not miscarried.

A similar injection of even 0.25 gm. ergotinine caused no miscarriage, but the animal died. Kraft, basing his conclusions on the experiments of Jacquet, says that the therapeutic use of ergot in exciting intense uterine contractions cannot be traced to the alkaloids, and that the alkaloids are convulsants, but that the bluing of the cock's comb may be due to hydroergotinin. However, Vahlen, who tested a sample of ergotinine sent by Kraft, found it practically non-toxic. The secalonic acids proved physiologically inactive.

It must be confessed that considering the physiological data which Kraft presents, one would not feel convinced that these compounds represented the physiological activity of ergot, because while the pregnant rabbits aborted after the injection of hydroergotinin, yet these animals showed marked constitutional symptoms, convulsions, etc., and it might be urged that abortion was only one feature of an intoxication. Again, by using glacial acetic acid and dilute alkalies as solvents for his bases, one is inclined to trace at least a portion of the action to decomposition products of the bodies brought about by such solvents.

While Kraft was carrying on his work, independent investigations on the same subject were being pursued at the Wellcome Research Laboratory of London. The first paper on this subject from that institution was published by Barger,[70] Carr and Dale in 1906, shortly after Kraft's original paper appeared. These investigators isolated a crystalline base which they named ergotinin and assigned to it the empirical formula $C_{35}H_{39}O_5N_5$. It proved to be Tanret's crystalline base. This alkaloid formed amorphous salts and was found to be physiologically inactive, thus corroborating the experiments of Kobert and Meulenhoff. They also isolated an amorphous base which they named ergotoxin. It was shown to have the composition $C_{35}H_{41}O_6N_5$. From it they succeeded in making a number of crystalline salts, especially an oxalate, hydrochlorate, hydrobromate, and a phosphate. The free base, unlike ergotinine, was soluble in dilute sodium hydrate solution. They examined a sample of hydroergotinine sent by Kraft and found it to be identical with their ergotoxin. Vahlen claims, however, that

the toxicity of ergotoxin and hydroergotinin differed too much for them to be the same compound. Meulenhoff had a similar experience but his experiments may be objected to on the ground that he was not using the purest products of these investigators.

The intravenous injection of .0005 to .001 gram of ergotoxin into a pithed cat, under artificial respiration, caused persistent rise in the systemic blood pressure, without a preliminary fall. Dale noted that after such an injection adrenalin failed to cause an immediate rise in blood pressure and showed what he called a "reversal in action," that is, a fall in blood pressure. In doses of a few milligrams, ergotoxin produced the typical bluing of the cock's comb and the uterine contractions in pregnant animals characteristic of ergot. The injection of 2 mg. of ergotoxin dissolved in dilute NaOH, into the ear vein of a rabbit, was followed in one case by dry gangrene of the ear. Unlike Kobert's cornutine, it produced no convulsions in frogs.

Barger and Dale at first believed, as did Kraft, that the active alkaloid was a hydrated form of the inactive one, and they adopted Kraft's view that each base could be converted into the other at will. The transformation of the inactive alkaloid into an active form was supposed to be accomplished by heating in dilute phosphoric acid. A more careful study has shown that this process does not yield ergotoxin phosphate, as was originally supposed, but a phosphate of ergotoxin-ethyl-ester. This has some physiological activity, so that in working with such solutions one is apt to be misled in attributing the action to this base. Ergotoxin thus contains a carboxyl group and the relation between the inactive and active alkaloids is that of a lacton. Barger and Dale believe the basic bodies isolated by Keller and also by Dragendorff to be mixtures of inert ergotinin with ergotoxin.

They soon noted that all of the physiological activity of ergot could not be explained on the basis that ergotoxin was the sole active principle, but that there must be some water-soluble one to which most of the activity of ergot was due. In investigating the pressor action of putrid meat Barger and Walpole found it was due to p. oxyphenylethylamin,

$$HO\langle\overline{\underline{\quad\quad}}\rangle CH_2CH_2NH_2, \text{ isoamylamin, } \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!\overline{\underline{\quad\quad}}\!\!> CH,\ CH_2NH_2,$$

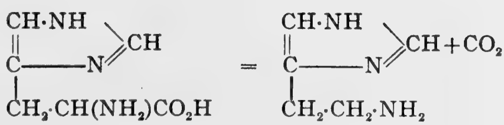
and phenylethylamin, and at once suspected some of these bodies to be the missing principles in ergot. They found p. oxypheny-

lethylamin, phenylethylamin and isoamylamin to be present in ergot. Para-oxyphenylethylamin can be shaken from water into ether provided sodium carbonate is used, but not by means of NaOH. Barger and Dale freed it as a benzoyl compound. The rise in blood pressure following the injection of ergot preparations was almost entirely due to the first constituent; the other two played only a subordinate rôle in the activity of ergot. They believed the first to be derived from tyrosin, while the others were traced to leucin and phenylalanin, respectively. Para-hydroxyphenylethylamin produces a rise in blood pressure much like adrenalin, only weaker. This similarity in action might be expected from the close chemical relationship with adrenalin, which may be represented as

$$\begin{array}{l} HO \\ HO\langle\_\_\_\rangle CH(OH)CH_2NHCH_3. \end{array}$$

Unlike adrenalin, this body is active when administered by mouth and produces no glycosuria. Isoamylamin and phenylethylamin have a similar action but less marked. Both compounds exert qualitatively the same kind of action on the true sympathetic system as adrenalin. Dale and Dixon say that " Both p. hydroxyphenylamin and isoamylamin were found to cause contractions of the uterus and vagina of the rabbit in all functional conditions," and the injection of either base would bring on labor in pregnant animals. Like adrenalin, p. oxyphenylethylamin causes inhibition in the non-pregnant uterus of the cat, and causes contraction in the pregnant uterus, however, it is much less toxic.

Kehrer noted that certain extracts of ergot produced an intense activity on the non-pregnant uterus of the cat, and that it was the dialyzed ergotin of Wernich which especially showed this action. This preparation is made by a slow process of dialysis, which suggested that it was due to the action of micro-organisms. The evidence at present points to β-iminazoylethylamine[71] as the compound to which this action is to be traced. This compound is derived from histidine by the elimination of carbon dioxide, in the same manner as p-hydroxyphenylethylamin is derived from tyrosine. Thus histidine



One month previous to the appearance of Barger and Dale's paper on β-imidazoylethylamine,[71] Kutscher had fractioned from ergot, by means of silver nitrate and ammonia, a derivative of histidin which was found to produce a marked fall in blood pressure in rabbits. He suspected it to be imidazoylethylamin, but found this latter would produce a rise in blood pressure while the base he obtained produced a fall and on this basis argued against its identity. The difference in the views of these investigators can be explained as due to differences in the animals used for testing their compounds.

Recently another active principle has been found in ergot by Engeland and Kutscher. This has been found to be agmatine, a base which Kossel[72] found in herring roe. Agmatine is related to arginine in the same manner as β-iminazoylethylamine is related to histidin.

According to the latest view, the action of ergot in bluing the cock's comb is due to ergotoxine, while the blood pressure raising action is mainly due to p. oxyphenylethylamin, although ergotoxine plays a part in it. Parahydroplyphenylethylamine is difficult to isolate, and the amount present has not been determined chemically, but by physiological tests it is estimated that 1 kilogram of ergot will yield a few decigrams of this substance.

The important problem now is whether ergotoxin, on decomposition, will yield these various pressor amines, and if not, are they all decomposition products of a common mother substance? Should this be so, this body remains to be isolated.

Resumé.

Investigators have long recognized in ergot the presence of two bodies which have been designated as alkaloids. The specific alkaloid, ergotoxin, is present in such small quantities in ergot that we cannot trace the entire therapeutic action of ergot to this compound alone. It would be well to decide whether the action of ergotoxin is not really due to an amino group. The evidence at present points to the fact that ergot owes its activity to the presence of various basic amino compounds, and this is supported by the fact that only fresh ergot is official in certain pharmacopœias, as it is known that ergot rapidly degenerates with the formation of tri-methylamine. It is interesting to note

that practically every preparation introduced by chemists or pharmacologists has been endorsed by some clinicians as useful in labor. This may perhaps be explained on the basis that all such preparations have carried mechanically with them some of the active constituents of ergot, but the conditions under which labor pains intermit and recur are so little understood that it is rather difficult to always show the relation of ergot to such pains.

A good review of this literature can be found in A. Bennecke. Der heutige Stand der Mutterkornfrage. *Archiv. f. Gynækol.*, vol. 38, p. 669, 1907.

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THE KEEPING QUALITIES OF ERGOT AND ITS FLUID EXTRACTS.

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Drugs are the doctor's tools. If a carpenter's tools are of poor steel, they will not take a fine edge, and cut but slowly; in ordinary work, with soft wood, the carpenter can manage to make some progress, even with comparatively poor tools, but when an extra hard piece of timber must be worked the edge of the soft steel will turn, and the tool will no longer cut at all. In an analagous way the physician under ordinary conditions, in the less serious complaints, may make some sort of progress even with drugs of inferior quality, but in an emergency, when life is perhaps hanging in the balance, it is essential that he have remedies on whose potency he can rely. Ergot is among those drugs which are frequently employed in conditions of immediate danger, and if pharmacy is to be a true handmaiden of medicine she must use her utmost endeavor to supply the physician with reliable preparations of ergot.

It has long been known that crude ergot was liable to deterioration. The United States Pharmacopœia says "after being kept more than one year it is unfit for use." While this statement is a proper recognition of the instability of the drug, as a legal standard it is a little extreme. Under present commercial conditions it is often impossible to obtain ergot which conforms strictly to the United States Pharmacopœia. The ergot crop is harvested chiefly during the month of August, and after collection, the bulk of the crop is sent to the large English exporters from whom it is imported into this country, and usually does not appear upon the American market until about January. It is, therefore, very evident that any ergot which is bought between the months of August and January must be more than one year old. Under the most favorable conditions, therefore, during only seven months of the year can the pharmacist possibly obtain ergot which is strictly U.S.P. Moreover, he has no means of being sure than the jobber from whom he buys his ergot is supplying him with the latest crop. There is reason to believe that some importing houses in New York keep their ergot, if not disposed of, for several years. I have had in my possession a

sample of crude ergot which was obtained from a large London importer accompanied with the statement that they had had it for three years and that they obtained it in turn from a New York firm who, to their certain knowledge, had had it for at least four years, and when we remember that the New York firm must have imported the ergot from Europe, so that it was at least one or two years old when they got it, it is evident that this sample of ergot was nearly, if not quite, ten years old. The specimen consisted largely of granular detritis, evidence of the ravages of insects, and the letter, commenting upon the appearance of it, stated with a delicious näivété: "If sifted it would look presentable, but could be saleable at current prices only if a scarcity came along, or if wanted for a cutting contract for some institution!"

Sad as it is to contemplate this disregard of our national standard, it becomes horrifying when we consider the justness of that standard, and remember the uses to which the drug is put. Grünfeld obtained a freshly gathered sample of ergot which he tested at various intervals during a year. He found that in October it required twice the dose to produce the coxcomb reaction that it did when gathered in August, that by February it required eight times the dose, and by June no dose would produce the characteristic effect. He does not state definitely what precautions were observed in keeping the ergot, and my own experience would lead me to believe with proper care crude ergot can be preserved more successfully than in his experiments. His work shows, however, the absolute necessity of using as fresh ergot as can be obtained.

There are two causes for the loss of activity in ergot: (1) the attacks of insects, and (2) chemical change taking place in its active principles. In regard to the first, there is at present no positive evidence that, if the ergot is sifted, the whole grains which are left upon the sieve are inferior in quality to ordinary ergot. Moreover, it is comparatively simple to protect the drug against these enemies. A little chloroform vapor is all that is necessary.

Concerning the change which takes place in the active principles of the drug, we have little information as to the chemical nature of these alterations or how to prevent them. Basing my conclusions upon the results of a single experiment, I have advised that powdered ergot should be dried for 48 hours at a temperature of 37° C. and then hermetically sealed, a little chloroform being previously added to prevent the growth of any mites.

It is a common belief among pharmacists that the fluid extract of ergot is much more permanent than the drug itself, but a series of experiments which were carried out by Dr. Hofer and myself has convinced me that it is a preparation which cannot be kept indefinitely. Whether it deteriorates more rapidly or less rapidly than the drug itself, I am not prepared to state, but I am satisfied that a fluid extract should not be kept more than a year under any conditions.

We investigated the problem of the influences which tended to hasten undesirable changes in the fluid extract of ergot in the following manner: Each sample of fluid extract of ergot as it was received from the maker was divided into three portions, one of which was immediately placed in an amber colored bottle which was completely filled so as to exclude any air, and hermetically sealed. The second portion was placed in a wide-mouthed container which was simply stoppered with cotton so as to keep out the dust, in this manner allowing free exposure to atmospheric influences, alcohol being added from time to time as it evaporated from the fluid extract. The third portion was kept in the bottle in which it was received from which, from time to time, small amounts would be removed for experimental purposes, the cork being replaced each time, in this way closely simulating the conditions in the ordinary pharmacy. It may be noted that these bottles were kept at room temperature and many of them through the summer. The following table shows the average loss per week of sphacelotoxin when assayed by the method described by me. (AMERICAN JOURNAL OF PHARMACY, May, 1909, page 215.)

I have included also the figures obtained by Grünfeld for crude ergot. As we found that the rate of deterioration was not constant, I have divided the table into two portions, the first of which gives the average loss of all the samples which were kept for from five to fifteen weeks, and the second, those which were kept sixteen to twenty-five weeks.

	5–15 weeks	16–25 weeks
Open	6.4% loss per week	2.5% loss per week
Corked	2.6% " " "	1.5% " " "
Sealed	1.6% " " "	1.3% " " "
Grünfeld	6.2% " " "	3.5% " " "

In the paper published by Doctor Hofer and myself (*Archives of Internal Medicine,* October, 1910, page 388), we have brought

forward evidence which served to convince us of the reliability of this process of chemical assay. It is to be noted, however, that my conclusions concerning the deterioration of the fluid extract of ergot are not based purely upon this chemical evidence, but also upon a number of physiological tests. We have found that the loss of activity as measured by its power to raise the blood pressure occurred more or less harmoniously with the figures just quoted, although we have only four samples concerning which we have complete records of the rapidity of change in physiological power under varying conditions.

As to the details of keeping, I may say that with the exception of the sealed bottles, which were invariably of amber-colored glass, no effort was made to protect the drug against the effects of the light, as we wished, in the one instance, to imitate, as nearly as possible, conditions in the retail pharmacy, and in the other instance, to see how rapidly the fluid extract would lose strength under the most favorable conditions for such change.

There are prominent obstetricians who maintain that ergot is an inert drug, so unfortunate has been their experience with its use. It is manifest that the poor quality of ergot upon the market is robbing the medical profession of a very valuable tool, and endangering the lives of those patients whose physicians place too much confidence in this drug. There is, therefore, crying need for correction of this really horrible state of affairs. In view of the fact that there is still much difference of opinion as to the best methods of testing the activity of ergot, and also of the fact that none of these methods can be satisfactorily conducted by retail pharmacists,—while the method of chemical assay suggested by myself is simple enough for any pharmacist to carry out, modesty forbids me urging it as a universal test until its value has been confirmed by other observers,—it is essential that pharmacists do what they can to see that their fluid extract at least fully represents the crude drug from which it was manufactured. For this reason, I would vigorously urge: (1) that the fluid extract of ergot be marketed by wholesalers in packages of not over four fluid ounces, and *immediately after the completion of the percolation;* (2) that each bottle carry plainly upon the label the date of its manufacture; (3) that no pharmacist be permitted to dispense a fluid extract of ergot which is more than six months old.

THE RESPONSE OF GUMS AND SIMILAR SUBSTANCES TO MOORE'S REACTION.

By Torald Sollmann
From the Pharmacological Laboratory of Western Reserve University, Cleveland, Ohio.

The well-known reaction of Moore or Heller consists in the occurrence of a yellow to dark brown color, when glucose solution is heated with KOH or NaOH. The reaction also occurs at ordinary temperature, but much more slowly.

This test, which was introduced in 1844 by John Moore[1] and F. Heller, has been practically displaced by other sugar-tests. It is especially unreliable for small traces of sugar in colored fluids. In urine, for instance, Rosenfeld (*Deutsche medicin Wochenschrift,* 1888, p. 451) failed to obtain reliable results even with 0.5 per cent. of glucose. In a pure solution, the test is very much more delicate. In my hands, even 0.01 per cent. of glucose gave a faint yellow color, which, however, bleached almost completely in twenty-four hours. A 2 per cent. solution of glucose gave a mahogany color, which was not noticeably changed in twenty-four hours.

The depth of color is also determined by the amount of free alkali. Framm (quoted from Neubauer and Vogel, Analyse des Harnes, tenth edition, p. 100), found that 0.01 per cent. of dextrose gave a good reaction with 0.5 per cent. NaOH. With sodium carbonate I found only a slight degree of darkening.

The nature of the reaction and of the products formed by the decomposition of the sugar are not clearly understood, although they have been the subjects of careful investigation (*Cf.* Neubauer & Vogel, *l.c.*) ; the process is evidently complex, and probably varies with the conditions, and with the nature of the substances employed.

Aside from dextrose, the test gives positive results with many other carbohydrates. According to Neubauer & Vogel (*l. c.*) and Hammarsten (*Lehrbuch der Physiologischen Chemie*), it is given

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[1] I may take this occasion to correct some curious errors in citations of Moore's original paper. Neubauer and Vogel, and Marck's Reagentien Verzeichniss both give a wrong reference, namely *The Lancet,* ii, Sept. 26, 1844; after considerable search we located it in *The Lancet,* ii, Sept. 14, 1844, p. 751; even the index of *The Lancet* gives the wrong page (75)!

by the *pentoses* (xylose) and *hexoses* (dextrose, levulose); of the *disaccharides,* maltose and lactose give the reaction, but not saccharose. *Mucin* is also said to respond positive. Of the *polysaccharides,* glycogen and dextrin are practically negative, but may react after prolonged heating, which presumably decomposes them. Starch is negative; so also is inosit.

All *aldehydes* which I have tried react positive (acetaldehyde, paraldehyde, formaldehyde, benzaldehyde and cinnamic aldehyde).

In all the preceding instances, the substances which give positive results reduce Fehling's solution, and those which react negatively to Moore's test also fail to reduce the copper.

On applying these tests to a number of gums and similar substances, I found a somewhat different behavior, which I have not seen recorded: These gums (*acacia, tragacanth,* and *cherry gum*), as also, *agar, cetraria,* and *chondrus,* give a golden or brownish-yellow color on heating with sodium hydroxide solution; but they do not reduce Fehling's solution even on prolonged heating.

As many of these may contain reducing sugar, they must be thoroughly washed (sometimes for several days). Even then there might be a suspicion that Moore's test is more delicate than Fehling's, but I have convinced myself that a dextrose solution which gives the Moore's test much more faintly than the agar solution, nevertheless gives a very plain precipitate with Fehling's test. With the difficulty soluble gums, the Moore's reaction can be best observed by heating the soaked substance directly with the reagent. I have applied the same technic to the Fehling's test, using one part of Solution A to three parts of Solution B. The results were negative, except with occasional specimens, which were presumably not sufficiently washed.

In the case of cetraria and cherry gum, the Moore's reaction was applied separately to the portions soluble and insoluble in water. The insoluble residue gave negative results. Cornstarch and glycogen did not give the Moore's reaction.

After heating with dilute acids (which converts gums into hexoses and dextroses) all these substances reduced the Fehling's solution.

THE EXTEMPORANEOUS PREPARATION OF MEDICATED GAUZES.

By George M. Beringer, Jr., P. D.

A few years ago the writer was called upon to prepare iodoform gauze bandages for an emergency order. This led to an examination of the literature upon the subject and experimentation upon improved methods for the preparation of such gauzes as are in common use. The results of the investigation are presented in this paper.

The earliest type of antiseptic gauze was that of Lister, made by soaking the material in a melted mixture of resin, paraffin and phenol. It is needless to say that such a "messy" preparation as this has long since passed from the American market. Many recent foreign works, and a few of our own, however, still retain the formula. Some, also, give a similar formula for the preparation of iodoform gauze, and the common method practised to-day is to distribute the iodoform over the surface of the gauze in the form of a starch paste suspension with glycerin. While this is better than the resin method, I believe that, aside from the required antiseptic, the less foreign material contained in a surgical dressing the better. Such material not only lessens the absorbent qualities, but may be irritant and, surely, restrains the activity of any antiseptic with which it may be combined.

Another point worthy of note is the incompleteness of many of the published formulas. One authority gives a formula for bichloride gauze. The amount of liquid directed for impregnation is one fluid ounce and contains 2 grains of mercuric chloride. *No amount of gauze is specified.* If the resulting preparation is to be of the usual 1 to 1000 strength, about 2000 grains of gauze will be required. The amount of liquid directed will hardly perceptibly moisten this, yet the directions are "*Immerse for twelve hours*"—"*Wring out*" and "*Allow to dry* as far as the glycerin will permit."

The first rational method appears to have been proposed by H. Helbing in 1889. He recommended ether or a mixture of ether and alcohol for the preparation of an extended list of gauzes. This was ideal in so far as no foreign material remained in the finished product, but the cost of the solvent, the danger from fire, and the unpleasant effects upon the operator precluded any extended com-

mercial application. However, in recent years, the reduced cost of ether and other solvents and the improvement of mechanical appliances for manipulation should have caused a general adoption of the method, but it seems to have been overlooked.

In the case of the iodoform gauze bandages first mentioned, ether was tried, but had to be abandoned, because of fire risk and its effects upon the operator. A solvent similar in diffusive properties to ether was sought and found in acetone. The tightly rolled bandages were saturated to the core in a few minutes after pouring the solution upon them. Furthermore, they dried perfectly and evenly as fast as they could be rewound. The same method has been applied to a number of other gauzes with equal success. The vapors do not seem to have any ill effect upon the operator.

When one remembers how long the name absorbent gauze has been used, it seems strange that a method of preparation based entirely upon the absorbent qualities has not been more generally used. Yet the majority of the published formulas direct an excess of liquid to be applied and subsequently removed by expressing to a given weight, and drying, losing sight of the fact that an amount of liquid just short of saturating the material would quickly and evenly diffuse, and evenly distribute the medicament. The application of this principle prevents the uneven distribution of the medicament as caused by the evaporation of a large amount of liquid, when heavy and slowly volatile from the lower, or when light and quickly volatile from the upper portions of the material suspended for drying. Obviously, it would have the added advantage of lessening the exposure of the product to septic contamination, as well as that of bringing it into the class of extemporaneous preparations by the saving in time effected.

Before proceeding with the individual formulas, it might be well to describe the gauze used and the necessary precautions to secure asepsis, even though they present nothing new. The older directions required the removal of the resins and fats from the gauze by solutions of soda or potassa and its bleaching by chlorinated lime or soda. It was then directed to be washed with hydrochloric acid and finally with water. Suitable material can now be had, already prepared, in the market. A satisfactory product contains about twelve threads to the centimetre both on the woof and on the warp, and is conveniently used in widths of about 90 cm. (1 yd.). One metre of this weighs about 25 Gms. It should be free from

chlorine and starch or gum-like material. According to the British Pharmaceutical Codex, 1 Gramme, when incinerated, should yield "practically no residue."

It is safer to prevent contamination, as far as possible, than to depend entirely upon sterilization for an aseptic product. The tables, floor and all other possible portions of the room where gauzes are to be prepared should be scrubbed with hot lye solution containing phenol. The top of the work table should be preferably of glass, but, if not, should be thoroughly scrubbed and finally washed with a 1–500 "bichloride solution," and covered with sheets of sterilized parchment paper before any dressings are placed upon it. The hands and nails of the operator should be scrupulously clean and washed, just before handling the material, in a 5 per cent. phenol solution. The clothing and hair should be covered with garments or wrappings of sterile muslin or gauze. Also, any objects not capable of being moved from the neighborhood of the work, and not needed for it, should be covered with sterile cloths. Jars, rods and all other materials should be sterilized where possible by boiling in water for fifteen minutes. Cartons and paper for packing and wrapping should be heated in an oven for one-half hour at a temperature of 120°–150° C.

The gauzes on the market, both plain and medicated, are in two forms—moist and dry. Hence directions for both are given. The moist forms seem to have the preference of most surgeons. They are more readily sterilized in that condition, are more pliable and suitable for packing wounds and cavities, insure more rapid drainage, and have less tendency to adhere to the wound surfaces.

Plain Absorbent Gauze, Dry.

The gauze should be cut into convenient lengths and rolled or folded into suitable bundles, wrapped in sterilized parchment paper and placed in a steam bath for one half-hour. It should then be removed and placed in previously sterilized cartons or wrapped in sterilized tough, heavy paper.

Plain Absorbent Gauze, Moist.

The gauze should be cut into suitable lengths, then sprinkled with sterilized distilled water containing 5 per cent. of glycerin and packed in previously sterilized amber glass jars. The filled jars,

with the caps loosely placed, should then be resterilized in a steam bath for one half-hour, after which they should be immediately sealed.

IODOFORM GAUZE, 10 PER CENT., DRY.

Iodoform	10 Gm.
Acetone	100 c.c.
Sterile gauze	100 Gm.

Dissolve the iodoform in the acetone and pour over the gauze loosely placed in a sterilized jar, or other suitable container, fitted with a close cover. Cover and allow to stand about fifteen minutes or until evenly moistened. Remove from the jar and drive off the acetone by waving in the air. Immediately wrap in sterilized parchment paper. Resterilize in steam bath for fifteen minutes and then enclose in a tight carton, or tough paper wrapper, previously sterilized.

IODOFORM GAUZE, 10 PER CENT., MOIST.

Prepare by taking iodoform gauze dry, as above, and sprinkling with freshly sterilized distilled water containing 5 per cent. of glycerin (about 75 c.c. wil be needed for each 100 Gm. of gauze). Allow to stand in a covered sterile jar till the moisture is evenly distributed. Pack into sterilized amber glass jars and resterilize, with lids of jars loosely placed, in a steam bath for fifteen minutes. Hermetically seal the jars immediately upon removal from the sterilizer.

Resterilization for only fifteen minutes is directed for iodoform gauze because of the ease with which iodoform is decomposed by heat.

Prepared in this manner, the iodoform is so firmly attached to the gauze that very little is washed off when immersed in water. With the starch paste suspension method, as previously mentioned, the secretion from a freely discharging wound, or the condensed steam from sterilization is sufficient to flush it from the material.

THYMOL IODIDE GAUZE, 5 PER CENT., DRY.

Thymol iodide	5 Gm.
Chloroform	25 c.c.
Acetone	50 c.c.
Sterile gauze	100 Gm.

Dissolve the thymol iodide in the chloroform and add the acetone. Prepare as directed for iodoform gauze, dry.

Chloroform is the best single solvent for thymol iodide, although no one solvent dissolves it entirely. Acetone is, however, the cheaper and, in the combination above, works satisfactorily.

Thymol Iodide Gauze, 5 Per Cent., Moist.

DRY THYMOL IODIDE GAUZE, 100 GM.

Water	75 c.c.
Glycerin	5 Gm.

Prepare as directed for iodoform gauze, moist.

Sublimated or Bichloride Gauze (Dry), 1–1000.

Mercuric chloride	.1 Gm.
Water	37.5 c.c.
Acetone	37.5 c.c.
Sterile gauze	100. Gm.

Dissolve the mercuric chloride in the acetone and water and proceed as under iodoform gauze, dry, but resterilize for one half-hour.

Sublimated or Bichloride Gauze (Moist), 1–1000.

Mercuric chloride	.1 Gm.
Water	75. c.c.
Glycerin	5 Gm.
Sterile gauze	100. Gm.

Dissolve the mercuric chloride in the water and add the glycerine. Proceed as directed for iodoform gauze, dry, but pack in sterilized amber glass jars. Have jar lids loosely placed, then put jars into steam bath and resterilize for one half-hour. Hermetically seal immediately upon removal from the sterilizer.

Phenolated or Carbolized Gauze, 5 Per Cent., Dry.

Phenol, crystals	5 Gm.
Acetone	50 c.c.
Water	50 c.c.
Sterile gauze	100 Gm.

Mix the acetone and the water, add the phenol, and proceed as for iodoform gauze, dry. Resterilization is used for only fifteen

minutes in this case because of the ease with which the phenol may be volatilized through the wrapping. While a small amount of moisture remains in the product when finished, it will dry rapidly after packing.

PHENOLATED OR CARBOLIZED GAUZE, 5 PER CENT., MOIST.

Phenol, crystals	5 Gm.
Acetone	50 c.c.
Water	50 c.c.
Glycerin	5 Gm.
Sterile gauze	100 Gm.

Mix the acetone, water and glycerin and dissolve the phenol in the mixture. Proceed as for iodoform gauze, dry, but pack, upon removal from impregnating jar, into sterilized amber glass jars and resterilize in a steam bath for one half-hour, having the lids of the jars loosely placed. Hermetically seal immediately upon removal from the sterilizer.

BORATED GAUZE, 10 PER CENT., DRY.

Boric acid	10 Gm.
Water	100 c.c.
Sterile gauze	100 Gm.

Dissolve the boric acid in the water by heat and proceed as for iodoform gauze, dry, excepting that the material should be kept at the temperature of boiling water till the moisture is evenly distributed, and then pack without further drying. Resterilize for one half-hour.

BORATED GAUZE, 10 PER CENT., MOIST.

Boric acid	10 Gm.
Glycerin	5 Gm.
Water	100 c.c.
Sterile gauze	100 Gm.

Dissolve the boric acid in the glycerin and water with the aid of heat. Proceed as for above, but pack in jars and finish as under iodoform gauze, moist, excepting that resterilization should be continued for one half-hour.

Picric Acid Gauze, 2 Per Cent., Dry.

Picric acid	2 Gm.
Water	50 c.c.
Acetone	50 c.c.
Sterile gauze	100 Gm.

Dissolve the picric acid in the acetone and water and proceed as under iodoform gauze, dry.

Picric Acid Gauze, 2 Per Cent., Moist.

Picric acid	2 Gm.
Glycerin	5 Gm.
Water	50 c.c.
Acetone	50 c.c.
Sterile gauze	100 Gm.

Dissolve the picric acid in the glycerin, water and acetone and proceed as for phenolated gauze, moist.

All gauzes for medication should be sterilized just before being used. This should be preferably, by dry heat at a temperature of 120°–150° C. for one half-hour, as many of the moistening liquids cannot be satisfactorily applied to any but dry material.

The amount of solution required for the impregnation of a given amount of gauze will vary slightly according to the number of threads to a given unit and the tightness of twist of the fabric.

Glycerin and acetone are not miscible, except upon the addition of water. Hence, it will be noted that gauzes prepared with material insoluble in water are moistened, where required, with glycerin solutions after impregnation.

In working out these formulas the question as to method of figuring the percentages arose. It will be noted that the percentage of medicament is based in each case upon the amount *added* to 100 parts of dry gauze. It is obvious that this furnishes the most convenient and most satisfactory means of figuring. The generally adopted method of parts *in* 100 parts of finished product, would be uncertain because of the variability of the moisture content through sterilization. Then, too, the weight of gauze taken is never exactly that given in a formula, but, in the nature of the case must be either a fraction or a multiple of the same and, often, an exceedingly inconvenient figure for calculation. For instance, work-

ing with 273 Gm. of gauze and a formula based upon 10 parts in 100 of finished product, 30.33 parts of medicament would be required. With the proposed method of 27.3 parts would be required, an amount easily and evenly calculated and weighed. Furthermore, if analytical methods are to be applied, it is much easier to remove the added material and figure upon a fixed remainder than upon an uncertain total weight. In the German "Erganzungsbuch" a formula is given which calls for 110 parts of iodoform to 1000 parts of gauze. There has, apparently, been an attempt to harmonize the two methods by the addition of an extra 10 parts in the amount of iodoform directed, apparently, in order to make the finished product exactly 10 per cent. This is, of course, not the result. We often see the kitten chasing his tail. But scientific authority rarely gives us the opportunity of witnessing a similar endeavor upon its part.

A few formulas for gauzes were given in a previous edition of the National Formulary, but were omitted in the last revision, probably because, as there directed, they could not be satisfactorily prepared by the pharmacist. Then, too, they were not of the character demanded by modern practice. The writer believes that some of the submitted formulas might be admitted into that work with advantage. It has been argued again and again that official recognition would be a mistake, because the pharmacist lacks the facilities, and it has been hinted that he has not the intelligence and training necessary for the careful preparation of surgical dressings. These arguments, to say the least, are not very complimentary to the ingenuity and ability of the American pharmacist, especially in view of the fact that his brethren in Germany, Austria, Switzerland, Belgium, the Netherlands and Italy, prepare such products from formulas in their respective pharmacopœias.

ABSTRACT OF REPORT OF THE COMMITTEE ON QUANTITATIVE METHODS

Division of Pharmaceutical Chemistry of American Chemical Society.

Your Committee begs to offer the following report of work which has been done since the last meeting (July, 1910). In the search for suitable assays for the various mercury salts included in the U.S.P., for which standards of purity are laid down and no assay processes are given, investigation was made of a number of existing methods as indicated below.

In order that you may know the method of working of the Committee, we give an outline of the plan pursued in this case. The Chairman sent out requests to the members of the Committee for suggestions as to methods suitable for general application to mercurous and mercuric salts. After going over the suggestions received, the following methods as proposed were again submitted to the Committee, together with samples of Mercurous Chloride and Mercuric Iodide. The methods as submitted are as follows:

Method No. 1.

Suggested by Mr. L. A. Brown.

(See Schimpf—Volumetric Analysis, page 408.)

Applicable to mercurous iodide, chloride, bromide, and mixtures of mercuric and mercurous salts.

Weigh out sample of about 0.5 gramme, place in Erlenmeyer flask of about 300 c.c. capacity, add 10 c.c. potassium iodide solution containing 2 grammes KI; rotate and quickly add 50 c.c. N/10 iodine solution by means of a pipette, agitate until all of the sample is in solution. Then run in N/10 $Na_2S_2O_3$ solution until all the free iodine has been removed, using starch solution if desired.

Reaction—$2HgCl + 6KI + I_2 = 2K_2HgI_4 + 2KCl$.

By mixing the HgCl with the solution of the potassium iodide immediately before adding the iodine solution, the insoluble salt goes into solution more quickly.

METHOD No. 2.

Suggested by Mr. L. A. Brown.

(Merck's Report, 1908, page 57.)

Applicable to mercuric chloride, iodide, cyanide, nitrate, oxide, ammoniated mercury, metallic mercury, and preparations of mercury such as ointments of mercury, ammoniated mercury, nitrate, and oxide; solution of mercuric nitrate, Donovan's solution, plaster of mercury, etc.

Dissolve one gramme of the sample (*e.g.*, $HgCl_2$) using one or two grammes of potassium iodide if necessary, in sufficient water to make 100 c.c. of solution.

Take 20 c.c. aliquot, add 1 gramme KI, 5 to 10 c.c. of 10 per cent. KOH sol., and 10 c.c. of water containing 2 or 3 c.c. of formaldehyde solution. Mix thoroughly and place on water-bath for about 10 minutes, or until supernatant liquid settles clear; then decant off through a small filter, washing residue with two portions or more of water, decanting through filter as before.

Dissolve the small amount of metallic mercury off the filter by means of a few drops of hot diluted nitric acid (1 : 1), washing the filter with a few c.c. of water to remove all traces of mercury. Collect filtrate and washings in the beaker containing the Hg, adding more nitric acid if necessary to secure solution of the mercury. Evaporate to about 2 or 3 c.c. on a water-bath, then dilute with water and transfer to a 100 c.c. flask, rinsing out beaker with successive amounts of water sufficient to make 100 c.c. of the solution.

Take an aliquot representing about 0.1 gramme of $HgCl_2$, add 25 c.c. of water, then a slight excess of 5 per cent. iodic acid solution, 5 c.c. being enough. This is added drop by drop, agitating all the while to secure complete agglutination of the curdy precipitate. As soon as the supernatant liquid is clear, filter and wash precipitate with three or four portions of water.

Dissolve precipitate off the filter with a few drops of diluted HCl, wash filter thoroughly, add 1 or 2 grammes of KI, allow to stand for about 5 minutes, then titrate the liberated iodine with N/10 $Na_2S_2O_3$.

Each c.c. of N/10 Thiosulphate = 0.0022405 gramme $HgCl_2$.

In the case of ointments, such as official ointments of mercury

and its salts, remove the ointment base by means of the proper solvent, dissolve the residue with nitric acid, and apply the method as given.

Method No. 3.

Suggested by Mr. B. L. Murray.

(See Smith—Electro-Analysis, pages 90 and 94.)

Applicable to solutions of mercury nitrate, the mercury oxides, metallic mercury, mercury with chalk, and possibly some of the other mercurial preparations.

Not applicable to calomel or corrosive sublimate.

Those preparations of mercury as found in the U.S.P., which can readily be brought into solution in nitric acid, are satisfactorily assayed for mercury by electrolysis.

The sample may well be of such a size that the final weighing of the metallic mercury will show a weight of about 0.250 gramme. The mercury solutions, or the dry preparations dissolved, are acidulated with 3 c.c. of concentrated nitric acid, diluted to 125 c.c., heated to 70° C., and then electrolyzed with a current of $N.D._{100}=0.06$ ampere and two volts. The metal will be fully precipitated in from 2 to 4 hours, and may appear as a uniform metallic coating upon the platinum dish, which is used as a cathode, or it may appear in shiny droplets. After the deposition of the material is complete, the mercury is washed with water, then with alcohol, then with ether, and finally dried a short time in the dessicator and weighed. The electrolyte remaining may be tested qualitatively for mercury to show that the deposition was complete.

The time may be materially shortened by the use of the rotating anode and mercury cathode.

Method No. 4.

Suggested by Mr. F. O. Taylor.

(See E. Rupp, Berichte, 1906, **39**, 3702.)

(See also Chem. Zeit., 1910, **34**, 229.)

A solution of the mercury salt, containing about 0.2 gramme of mercury in 25 to 50 c.c. of solution, is treated with excess of KI so that the HgI_2 formed redissolves. Render alkaline with NaOH; treat with 3 c.c. of 40 per cent. formaldehyde solution

diluted with 10 c.c. of water and let stand with occasional stirring for about two minutes. Acidify with acetic acid; add 25 c.c. of N/10 iodine and after all the precipitated mercury has combined with the iodine, titrate the excess with N/10 sodium thiosulphate solution.

Mercurous salts must be converted into mercuric before precipitation.

In the case of mercuric cyanide, sulphuric acid should be used instead of acetic in order to decompose any cyanogen iodide which may have formed.

Method No. 5.

Suggested by Mr. F. O. Taylor.

(See C. J. Pretzfeld—J. A. C. S., 1903, page 198.)

Estimation of Mercury as Arsenate.

The mercury must be present as a mercuric salt, and preferably as a nitrate, as mercuric arsenate is not precipitated from the chloride solution. A small amount of free nitric acid does not interfere with the accuracy of the results. To a cold solution containing about 0.25 gramme Hg in 100 c.c., add 20 c.c. of saturated solution sodium arsenate. The heavy yellowish-white precipitate of mercuric arsenate immediately forms and settles rapidly, but for greater accuracy the author of the method recommends that the solution stand for several hours; then filter through a Gooch filter, wash thoroughly with cold water and dry at 100°.

Method No. 6.

Suggested by Mr. F. O. Taylor.

(See same paper as above.)

Estimation of Mercury as Chloride.

To a solution of the mercuric salt, preferably in the form of a nitrate containing about 0.25 to 0.4 gramme Hg, add a slight excess of a mixture containing one drop of hypophosphorus acid to each c.c. of H_2O_2, and then immediately an excess of solution sodium chloride. Let stand for one hour, filter off the precipitated HgCl, wash thoroughly, dry at 100° and weigh.

Below, in tabular form are given the results obtained by different members of the Committee in using these methods.

Analysis of Mercurous Chloride.

Chemist	Method No. 1. Per cent.	Method No. 4. Per cent.	Special Method[5] Per cent.
Mr. L. A. Brown	100.10[1]		
	99.91		
Mr. B. L. Murray	98.94[2]		99.62[5]
	99.33		99.79
	99.25		
	99.35		
	99.23		
	99.19		
Mr. L. D. Havenhill	100.46[3]	99.84	
	99.71	100.04	
	100.01	99.62	
	100.04	99.84	
	100.18		
Mr. F. O. Taylor.	[4]		

Comments.

[1] Method is entirely satisfactory if closely adhered to.

[2] Method worked well, although some time was consumed in effecting solution in iodine.

[3] The factors seemed too large to permit of sufficient accuracy when working upon samples of close to 100 per cent. purity.

[4] (Mr. Taylor's results are unfortunately unavailable, but his comments are at hand.) The chief difficulty with this method is the dissolving of the mercury by the iodine solution, which is very often extremely slow. Aside from this, the method seems very good.

[5] Samples were dissolved in sodium sulphide solution and electrolized three quarters of an hour with 0.5 ampere, 4–5 volts, using mercury cathode and rotating anode. (See Jour. Ind. and Eng. Chem., vol. 2, page 481.) Results very satisfactory.

Analysis of Mercuric Iodide.

Chemist.	Method No. 2. Per cent.	Method No. 3. Per cent.	Method No 4. Per cent.	Method No. 5. Per cent,	Method No. 6. Per cent.
Mr. L. A. Brown	95.74[12]		99.67[26]		
			100.39		
Mr. B. L. Murray	79.17[13]	98.68	98.57[20]		
	86.36	99.38	99.38		
	81.50	98.52			
	86.04				
	62.01				
	80.82				

Chemist.	Method No. 2. Per cent.	Method No. 3. Per cent.	Method No. 4. Per cent.	Method No. 5. Per cent.	Method No. 6. Per cent.
Mr. L. D. Havenhill........	94.40 [14]	97.83 [8]	64.1 [15]	97.85 [23]	97.98
	94.19	97.94 [11]	98.64 [17]	93.10	97.84
	94.65	99.89 [11]	97.64 [17]	98.09	97.60
	91.88	98.86 [11]	98.80 [18]	94.00	97.51
	97.65 [6]	[9]	98.86 [18]		
	98.80 [6]		99.58 [18]		
	97.65 [6]		99.98 [19]		
	91.88 [7]		99.80 [19]		
	93.95 [7]		99.70 [19]		
			99.62 [19]		
			100.50 [19]		
			[21]		
Mr. F. O. Taylor...............	[16]	[10]	[22]	[24]	[25]

Comments.

[6] Precipitating and washing in dilute alcohol.

[7] Same solution as preceding [6] but washing with water.

[8] Dried at 50° C.

[9] Our work seems to indicate that there was a considerable loss of mercury, due to volatilization when the cathode was dried at a temperature of 50°.

[10] Unquestionably the electrolytic method is extremely accurate when used by one who is experienced and has at hand the proper apparatus, and it can also be made a very rapid method. It does not seem, however, to be suited to the requirements of pharmacopœial estimation, as at the present time one is much more likely to find the requisite skill and apparatus for making other forms of assay than the electrolytic, among those to whom these assays would be chiefly valuable.

[11] Dried in dessicator at room temperature.

[12] Mr. L. A. Brown: I got very poor results due possibly to two causes: (1) Mechanical loss of mercury in filtering after reduction. (2) Part of the mercury appears to come down in a colloidal condition and is lost in the filtrate. I have proven to my entire satisfaction that the reduction by formaldehyde in alkaline solution is quantitative, and what makes me believe that part of the mercury is in a colloidal form is that a *perfectly clear filtrate* will shown the presence of mercury by hydrogen sulphide if completely saturated.

[13] The method gave us uncertain results.

[14] Mr. L. D. Havenhill: The amount of water used in washing the precipitate of mercury iodate tends to vary the results.

[15] Thirty seconds with stirring for reduction.

[16] Mr. F. O. Taylor: We find this method inaccurate because of the distinct solubility of the mercuric iodate in water, which solubility may be proved by testing the filtrate from the mercuric iodate by hydrogen sulphide, when a very decided test for mercury can be obtained.

[17] Two minutes with stirring for reduction.

[18] Four minutes with stirring for reduction.

[19] Five minutes with vigorous shaking.

[20] Mr. B. L. Murray: In using this method we found that two minutes was not sufficient time for the reduction of the mercury by formaldehyde. Even five minutes was too short a time and a little heat was used to complete the reduction; but this we found reduced the mercury to such a condition that it was very hard to dissolve in the iodine solution.

[21] We found the time for reduction to be insufficient, also the stirring. Better, or at least higher results were obtained by vigorously shaking the mixture. The quantity of acetic acid used is indefinite. Our results, which are not herein reported, seem to show that the more acetic acid used, the lower are the results. We believe that the size of the factor is too large to permit of sufficient accuracy when working on samples that run close to 100 per cent. in purity.

[22] Here again the difficulty of dissolving the precipitated mercury in iodine solution is the chief drawback. With care the method can be made accurate, but it usually requires more time than a process of this kind should.

[23] In this method the mercuric iodide was reduced with formaldehyde in the manner indicated by the method of E. Rupp, dissolved in nitric acid and precipitated with sodium arsenate. It was noted that the precipitate of mercuric arsenate was not of uniform color. The higher results here reported were obtained from precipitates that were materially whiter in color than those (more yellow) precipitates yielding the lower results which were more yellow in color.

[24] Inaccurate results here may be attributed to the slight solubility of mercuric arsenate in water, which seems to be sufficient to render the method not very desirable.

[25] No careful work was done by me on this method, but only some preliminary tests, and it would appear that special care must be taken in the reduction of the mercuric salts and it is therefore preferable to use phosphorus acid instead of hypophosphorus acid.

[26] Contrary to previous observations I find this method to give good results if the reduction is carried out in the cold and not allowed to stand too long before adding iodine solution. If the reduced mercury is allowed to coalesce and form large globules the solution of the mercury in the iodine solution is *very* slow.

CORRESPONDENCE.

AMERICAN PHARMACEUTICAL ASSOCIATION.

AMERICAN JOURNAL OF PHARMACY,

GENTLEMEN:

Chairman Beal of the Council of the American Pharmaceutical Association has sent out the following communication:

J. W. ENGLAND,
Secretary of the Council.

"TO THE MEMBERS OF THE COUNCIL:

As a means of carrying into effect Resolution No. 31, relating to the raising of a fund for the liquidation of the indebtedness upon the home of the late Professor C. S. N. Hallberg, I have appointed the local committees named below, and suggested that they work in accordance with the following plan:

(1) That the several local committees be authorized to join with them such additional persons as they may select to assist in the soliciting of subscriptions.

(2) That subscriptions be solicited not only from members of the American Pharmaceutical Association, but from any others who may be interested in paying a tribute to the memory of Professor Hallberg on account of his distinguished services to American Pharmacy.

(3) That the names of all subscribers to the said fund, with the amounts subscribed, be published in the Bulletin of the Association.

(4) That the subscription be taken upon the form submitted herewith, and that all such subscriptions, when signed, and all cash contributions received by the solicitors, be forwarded to the Treasurer of the Association, Dr. H. M. Whelpley, 2342 Albion Place, St. Louis, Mo.

I am informed that the title to the Hallberg home is in the name of Mrs. Hallberg, and that there remains due upon the same approximately the sum of $3,500.00 payable in annual instalments of $500.00 each, with interest.

The Chairman will be grateful for additional suggestions, either as to the regulations concerning the taking of subscriptions or of names to be added to the several local committees, or to act in districts not represented in the list herewith submitted.

Respectfully submitted,

J. H. BEAL."

AMERICAN CHEMICAL SOCIETY.

Division of Pharmaceutical Chemistry.

The Division of Pharmaceutical Chemistry of the American Chemical Society held its Minneapolis meeting in the Chemistry Building of the University of Minnesota on December 29. The address of Prof. A. B. Stevens (Chairman) upon Pharmacopœial Standardization was especially interesting and timely, since Prof. Stevens is a member of the Committee of Revision of the Pharmacopœia, and Chairman of the Sub-Committee on Proximate Assays. The address outlined the work being done by the Sub-Committee mentioned and made clear the thoroughness and carefulness with which the Pharmacopœia is being revised. The new and improved methods of committee work were also explained.

The Report of the Committee on Quantitative Methods gave a resumé of the analysis of Mercury Salts by six different methods. The Committee has done valuable work and is being continued. The Report, although merely a report of progress, was ordered published in order that the greatest benefit may be obtained from the work of the Committee.

The papers read at the meeting were as follows: A. B. Stevens, Citro-Compounds of Iron; E. R. Miller and G. H. Marsh, Camphor in Oil of Sassafras; L. E. Sayre, Assay of Gelsemium; F. Klein, Rapid Determination of Sulphuric Acid with the Porous Clay Crucible; E. Kremers, Chemical Problems Suggested by the Cultivation of Medicinal Plants, (1) Stramonium.

The following officers were elected for the ensuing year: Chairman, B. L. Murray; Vice-Chairman, A. D. Thorburn; Secretary, F. R. Eldred. Members of Executive Committee: A. B. Stevens, L. F. Kebler.

B. L. Murray,
Chairman.

From the painting by Mr. Hugh H. Breckenridge.

MR. HOWARD B. FRENCH, PH.G.
President Philadelphia College of Pharmacy.

THE AMERICAN
JOURNAL OF PHARMACY

MAY, 1911

THE IDENTIFICATION OF COCAINE AND SOME COCAINE SUBSTITUTES.

By Francis J. Seiter and Frederic Enger.

During the last five years, a large number of specimens, containing cocaine, has been examined in this laboratory. This work was done for the Chicago police department, which has been striving to stamp out the illegal sale of cocaine to habitual users of the alkaloid.

The chief difficulty which presented itself in the analysis of the specimens was the small amount of material submitted by the police officers. The weight of an average specimen was approximately 0.1 gram. The specimens frequently contained acetanilide in amounts varying from 20 per cent. to 80 per cent. Some of the catarrh powders, *e.g.*, Dr. Gray's Catarrh Powder, contained but 8 grains of cocaine hydrochloride to the ounce. As in all these cases a portion of the specimen was reserved for exhibition in court, the quantity of alkaloid available for identification was so small as to render imperative the adoption of a scheme of analysis whereby the material might be economized without sacrifice of accuracy.

Many of the proposed tests for cocaine require considerable quantities of the alkaloid and yield results not characteristic of cocaine alone. Among these may be mentioned the tests with concentrated mineral acids, with or without the addition of oxidizers or other substances used in color reactions and the test involving the detection of the benzoyl group, which requires at least 0.2 gram,

according to Autenrieth.[1] This test is not reliable, however, as it is also given by alpha- and beta-eucaine, stovaine and, in fact, by any of the cocaine substitutes containing the benzoyl group.

The tests which fulfilled our requirements most satisfactorily, and which we adopted in our work, are based upon the following observations. Cocaine salts will react, under certain conditions, with gold chloride, platinum chloride, chromic acid and potassium

Fig. 1.

Cocaine chloro-platinate, x 100.

permanganate to form precipitates which, when examined under the microscope, are found to possess definite and characteristic crystalline forms.

The test solutions required are—1 per cent. solutions of gold chloride, platinum chloride and potassium permanganate and a 5 per cent. solution of chromic acid.

The alkaloid, isolated in the usual ways, is converted into the hydrochloride and made up to a 2 per cent. solution. A small por-

[1] Autenrieth, Auffindung der Gifte, 3 Aufl., page 79.

tion of this 2 per cent. solution, say ½ c.c., is set aside for the permanganate test. The remaining solution is diluted with an equal volume of water, forming a 1 per cent. solution. Portions of ½ c.c. of this solution are reserved for the platinum chloride and chromic acid tests. To a third ½ c.c. portion of the 1 per cent. solution is added 1 c.c. water and the resulting liquid used for the gold chloride test.

FIG. 2.

Cocaine-chloro-aurate, x 100.

POTASSIUM PERMANGANATE TEST.[2]

To ½ c.c. of a 2 per cent. solution of cocaine are added five drops of permanganate test solution. A precipitate is formed consisting of violet-red, rectangular plates. The other common alkaloids either immediately or slowly reduce the permanganate without forming crystalline precipitates.[3] This is also true of the cocaine substitutes, holocaine, acoine, and euphthalmine, which almost in-

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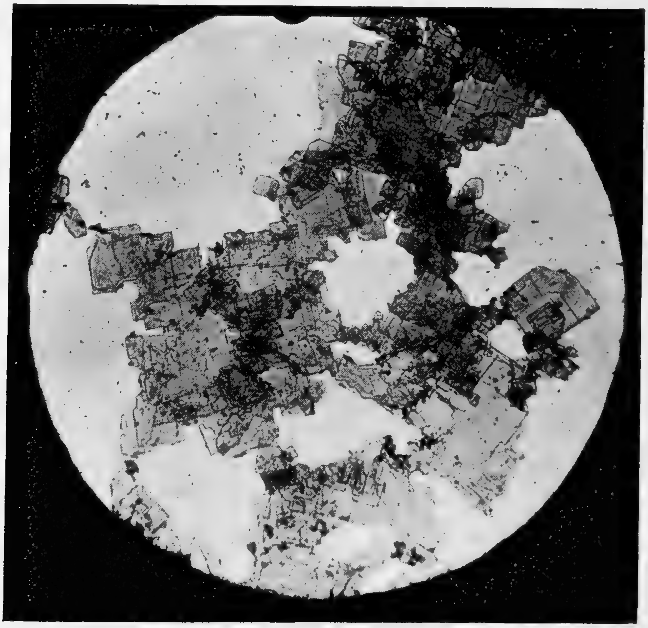
[2] F. Giesel, *Pharm. Zeit.*, 1886, p. 132.

[3] Allen, Comm. Org. Anal. 2d Ed., vol. III, pt. ii, p. 144.

stantly reduce the permanganate. Alpha- and beta-eucaine and stovaine do not reduce the permanganate immediately, resembling cocaine in this respect. No crystals, however, are formed in these cases.

The permanganate reaction requires a fairly concentrated solution of cocaine, but there is no difficulty in obtaining the character-

FIG. 3.



Cocaine permanganate, x 100.

istic violet-red plates in a 2 per cent. solution. "With a one per cent. solution, the crystals (of cocaine permanganate) only form as evaporation takes place."[4]

PLATINUM CHLORIDE TEST.[5]

To ½ c.c. of a one per cent. solution of cocaine are added two drops of platinum chloride test solution. The test tube should not be shaken, as larger and better formed crystals will result

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[4] Allen, Comm. Org. Anal. 2d Ed., vol. III, pt. ii, p. 276.
[5] A. B. Lyons, AM. JOUR. PHARMACY, lvii, No. 10.

when the solution is undisturbed. A buff colored precipitate is formed which, under the microscope, appears as large feathers or plumes, sometimes arranged in stellate pattern. In higher dilutions (1:600) crystals slowly form which "resemble carpet tacks." [6]

Alpha-eucaine, with the above test, gives bundles of fine needles; beta-eucaine, after 30 minutes, gives a few very large, broad leaves, rosettes and cubes; holocaine gives small stars; acoine gives an amorphous precipitate, while stovaine and euphthalmine give no precipitates. None of the precipitates yielded by the cocaine substitutes resemble the cocaine chloroplatinate in any way.

GOLD CHLORIDE TEST.[7]

To one c.c. of a dilute solution (1:300) of cocaine are added three drops of gold chloride test solution, avoiding shaking as in the case of the platinum chloride test. A precipitate immediately forms and slowly changes from the amorphous into the crystalline state. Under the microscope, the crystals resemble fern-fronds, generally with a stellate arrangement. In dilutions of 1:12,000, similar crystals form after long standing.

With the gold test, alpha-eucaine gives branching, twig-like crystals; stovaine gives large crystals resembling those of cocaine chloroplatinate in general structure, but differ in that the branches possess smaller branches, which is not the case with the cocaine chloroplatinate. Amorphous precipitates are given with beta-eucaine, acoine and holocaine. Euphthalmine gives no precipitate.

CHROMIC ACID TEST.[8]

To ½ c.c. of a one per cent. solution of cocaine are added two drops of chromic acid test solution and then concentrated hydrochloric acid, drop by drop with shaking, until the precipitate dissolves. After a short time, clusters of fine needles separate out and the solution remains yellow for several days.

Alpha-eucaine gives a precipitate which requires a large volume of hydrochloric acid for complete solution. The liquid remains yellow for several days but no crystals form. Beta-eucaine and stovaine behave like cocaine but no crystals separate out in either

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[6] Allen, *loc. cit.*, p. 275.

[7] A. B. Lyons, *loc. cit.*

[8] K. Metzger, *Pharm. Zeit.*, xxxiv, 697, also Allen, *loc. cit.*, p. 276.

Reagent.	Cocaine.	A-eucaine.	B-eucaine.	Stovaine.	Holocaine.	Acoine.	Euphthalmine.
$AuCl_3$	Fern-like crystals.	Twig-like crystals.	Amorphous ppt.	Branched crystals.	Amorphous ppt.	Amorphous ppt.	No ppt.
$PtCl_4$	Feathery crystals.	Fine needles.	Leaves, cubes and rosettes.	No ppt.	Small stars.	Amorphous ppt.	No ppt.
KM_nO_4	Violet-red squares. Slow reduction.	No crystals. Slow reduction.	No crystals. Slow reduction.	No crystals. Slow reduction.	No crystals. Immediate reduction.	No crystals. Immediate reduction.	No crystals. Immediate reduction.
H_2CrO_4	Fine needles. No reduction.	No crystals. No reduction.	No crystals. No reduction.	No crystals. No reduction.	No crystals. No reduction.	No crystals. Brown ppt. and solution.	No ppt.
Chlorine Water	No ppt.	Milky turbidity.	Dense turbidity.	Light turbidity.	Yellow turbidity.	Maroon ppt. and claret sol.	No ppt.

case. Holocaine gives a precipitate soluble in hydrochloric acid, but no crystals form and the solution turns green on standing. Acoine gives a precipitate soluble in hydrochloric acid. After a short time, a brown precipitate forms and the supernatant liquid becomes brown, slowly changing to green. Euphthalmine gives no precipitate with chromic acid test solution.

Cocaine solutions will yield crystals with chromic acid in dilutions of 1 : 1000.

The behavior of cocaine with the chromic acid test is not duplicated by any of the other common alkaloids.[9]

In addition to the above tests, the behavior of chlorine water with the cocaine substitutes has given valuable results which serve to differentiate between these and cocaine. To 1 c.c. of a one per cent. solution of alkaloid are added 2 c.c. of saturated chlorine water. Cocaine gives no precipitate; alpha-eucaine, a milky turbidity; beta-eucaine, a dense white turbidity; holocaine, a light yellow turbidity; stovaine, a light milky turbidity; acoine, a maroon precipitate and claret solution, and euphthalmine, no reaction.

The results of all the foregoing tests are appended in tabular form on the opposite page.

The micrographs, representing a magnification of 100 diameters, were kindly made for us by Mr. Carl S. Miner, Ellsworth Building, Chicago, for which we wish, in this place, to express our appreciation.

PHYSIOLOGICAL METHODS FOR THE STANDARDIZATION OF DIGITALIS.

By Charles C. Haskell, A.B., M.D., Indianapolis, Ind.

It seems to be generally admitted that there is no satisfactory method for the chemical assay of the drugs of the digitalis series. Reed[16] and Vanderkleed claim to have found an agreement between the values obtained for digitalis preparations through physiological tests and those obtained through determination of the digitoxin content, but their experience is practically unique, other investigators being able to see no such agreement. Inspection shows, moreover, that the results secured even by Reed and Vanderkleed are not at

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[9] Metzger, *loc. cit.*

all convincing. In view of this fact, much work has been done in the attempt to secure a satisfactory method of physiological assay for the heart tonics.

Changes in the blood pressure and heart rate of a mammal following the intravenous administration of digitalis are, in all probability, proportional to the therapeutic value of the drug. It has been shown, however, that this method of testing is not suited for accurate standardization of the drugs belonging to the digitalis group. The same preparation injected into different animals will cause different percentage increase in blood-pressure and decrease in heart rate; while if a standard be injected with the purpose of comparing its action with that of the preparation to be tested, this standard will modify the results, secured by the subsequent injection of the drug of unknown strength, owing to the fact that the digitalis bodies are very slowly destroyed or eliminated by the animal organism.

The perfusion of the isolated mammalian heart also offers a satisfactory qualitative test for digitalis, but the technic is difficult and Sowton [18] has shown that the method is not suited for quantitative determinations.

The methods now commonly advocated may be divided into:

I. Those upon frogs.
- A. Houghton's 12-hour method.
- B. Focke's method.
- C. One-hour method.

II. Those upon mammals.
- A. Guinea-pig method.
- B. Hatcher's cat method.

To Houghton [12] belongs the credit of first employing physiological tests for the commercial standardization of the heart tonics. The method which he proposed in 1898 and which, with slight modifications, is still employed, rests upon the determination of the minimum lethal dose of the drug for a frog, usually *Rana pipiens*. A series of frogs is injected, into the anterior lymph sac, with varying doses of the preparation to be tested; and at the same time, another series of frogs from the same lot is injected with a standard. At the end of 12 hours, the animals are examined. If the variation of dosage has been sufficiently great, certain of the animals are alive, while certain others are dead. A second series is now injected with

the smallest dose which proved fatal in the first case, and if the majority of these are dead at the end of 12 hours, this dose is accepted as the m. l. d.

Focke's[7] experiments seem to have been carried out on *Rana temporaria.* The animals are fastened to a board and the heart is exposed with avoidance of hemorrhage. The drug, in the form of an infusion, is injected into the femoral lymph sacs, and the time noted before systolic stoppage of the heart.

A factor V is then determined from the weight of the frog, size of the dose, and lapse of time before systolic stoppage of the heart.

The one-hour frog heart method was originated by Cushny[4] and is now much used by his pupils, Edmunds and Hale. (The method proposed by Fraenkel[6] in 1902 differs from this in several important details.) It resembles Houghton's method in that the frogs are injected in series and comparison is made with another series injected with a standard preparation. At the expiration of exactly 60 minutes, however, the animals are pithed and the hearts exposed. When just the proper dose or an amount slightly in excess has been injected, the heart presents a characteristic picture; the auricles purple and distended; the ventricle white, motionless, and contracted.

In 1908, Reed[16] revived the guinea-pig method for determining the strength of preparations of the "heart tonics." Laborde and Duquesnel,[13] in 1884, were apparently the first to use the guinea-pig in such tests, their investigations dealing with two samples of "digitalin," the solutions of the drug being injected subcutaneously or intramuscularly. In 1888, Gley[9] compared the toxicity of oubain and strophanthin, using guinea-pigs and other animals. When Houghton,[12] in 1898, published his method for the assay of strophanthus, he stated that he had employed guinea-pigs, as well as frogs and other animals, upon which to perform experiments.

Reed believes that frogs are unsuitable animals to employ in these tests, because they vary in their resistance to the drug according to season, species, and weight; while the guinea-pig "does not appear to offer so wide a variation." In the same year, Crawford[2] pointed out the unreliability of frogs, their powers of resistance depending upon season, sex, and room temperature. He considers that: "Dr. Reed, of Philadelphia, has made an important advance by using guinea-pigs, animals which are more resistant to injury."

Githens [8] is firmly convinced of the superiority, as experimental animals, of guinea-pigs over frogs. The latter are markedly influenced "by external surroundings, temperature, amount of moisture present in the cage, relation of time of feeding to time of injection, etc. The species of frog also makes a difference, and, according to many authors, the time of year." The guinea-pig, on the contrary, "shows no such variation." The use of a standard preparation for comparison with the preparation to be tested is unsafe, because the standard is "dependent on the keeping properties of a stock galenical, and these are exceedingly uncertain in many drugs."

Finally, the committee on pharmacological assay, of the Philadelphia branch of the American Pharmaceutical Association,[17] advocates the adoption of the guinea-pig method as the official method of assay for digitalis. Frogs, they state, vary according to species, season of year, and locality. "Guinea-pigs, on the other hand, are obtainable in all parts of the world . . . their susceptibility to digitalis, *so far as is known,* does not vary under ordinary conditions. Temperature, food, season, weight, and sex do not influence their reaction." The members of the committee are convinced that the use of a standard preparation is unsafe, because this standard may vary in strength and cause error in testing the preparation of unknown strength.

Granting that the guinea-pig is a better experimental animal than the frog, do the methods present any differences? In speaking of the frog methods, Reed [16] says: "It is, after all, only a toxic effect, and the fact that the frog dies with its heart in systole is not any more characteristic than the mammalian heart in diastole. In either case, the animal dies, and the cause of its death is the *action of digitalis on the heart.*" Crawford [2] also considers both frog and guinea-pig methods to rest upon the determination of the m. l. d. Githens [8] discusses the matter rather fully. "The physiologic action of these drugs, on which their therapeutic value depends, is mainly a stimulation of the heart, shown by more forcible contraction of its walls. The drugs kill either by inducing a state of constant contraction (death in systole) or by overworking the heart muscle to such an extent that it gives way to a more or less sudden exhaustion with relaxation (death in diastole). In either case the effect is primarily due to stimulation of the heart, and thus varies in accord with the physiologic or therapeutic activity.

. . . occasionally in mammals the respiration ceases before the heart has come to a standstill. *This does not indicate any direct action of the drug on the respiratory centres, but is due to interference with the function of the medulla, dependent on the disturbance of its blood-supply. The death is thus due to the stimulating action on the heart, however it may eventually occur.*"

The Philadelphia committee [17] find that the only essential difference in the methods is that the question of absorption plays an important part if frogs are used. They state that Edmunds and Hale showed "the fatal dose for 12 hours is about three-fourths of that for one hour. It is evident that the difference between the dose required to kill in one hour and that required to kill in 12 hours is largely a question of rapidity of absorption. Now, it may easily be that a preparation which is highly active may be, for some reason, comparatively slowly absorbed, so that the one-hour test is not only of activity of the drug, but of absorbability, which is manifestly not the purpose of the assay."

Hatcher [11] believes that the cat is especially suited for the assay of these drugs. By the intravenous administration of the preparation to be tested, a method simpler, cheaper, more accurate, and less time-consuming than those usually employed is secured.

The simplicity of this method is not very apparent, necessitating, as it does, anæsthetizing the cat, dissecting out the vein, and insertion of a canula. It has not been our experience that cats are cheap or easily obtained. According to the tables Hatcher gives, with digitalinum verum there was an error of 20 per cent.; with digitalin, of over 55 per cent.; with impure adonin, of 9 per cent. Further, in a note he says: " . . . we have found a number of cats which tolerated doses up to nearly 50 per cent. more than that stated." The actual time of one assay is 90 minutes, but when it is realized that a certain amount of preliminary preparation is needed, it is evident that running two animals, the minimum number from which reliable results could be obtained, will consume over three hours.

That these experienced pharmacologists should, after mature consideration, come to such conclusions is a fact that makes me hesitate to take a contrary view. It does appear, however, that certain points in favor of the frog methods have not been fully brought out; nor have certain important draw-backs to the mammalian method been given the prominence that is proper. Moreover,

some of the statements of Reed and Githens, unsupported by experimental proof, are rather at variance with the commonly accepted views regarding the pharmacology of digitalis.

To summarize the statements of the authors I have mentioned above, we learn that:

I. Frogs vary markedly in resistance to digitalis poisoning.

II. That the adoption of a standard is unsafe because of the uncertainty regarding the strength of this standard.

III. That guinea-pigs react with much uniformity to digitalis.

IV. That absorption plays an important part in the frog methods.

V. That guinea-pig and frog methods are lethal dose methods; death in both cases resulting from the action of the drug on the heart.

As suggested by Houghton, crystalline strophanthin, also known as strophanthin gratus or ouabain, is an ideal substance for a standard. Possessing, as it does, the characteristic "digitalis" action on the frog's heart, it is a definite chemical compound, and the question of variability of strength or deterioration does not come into play. By means of this ouabain, each frog lot can be standardized, and the possibility of error arising from uncertain reaction of the frog eliminated.

It is indeed commendable with what care some of the authors I quoted have scrutinized the frog methods in the effort to discover defects from the unfitness of the animal. The same amount of scrutiny has not, apparently been bestowed upon the guinea-pig. Reed[16] contents himself with saying that this animal "does not appear to offer so wide a variation"; Githens[8] says that it "shows no such variation"; while the Philadelphia committee[17] modifies its claim as to constant resistance in guinea-pigs by adding: "So far as is known."

In this connection, it is of interest to mention some of the results secured by Arms[1] in animal inoculations.

Two pigs inoculated with emulsion of nervous tissue from rabid dog: one developed typical paralysis on 11th day; second showed no evidences of injury and was normal at autopsy 13 months later. Two pigs inoculated with emulsion from another rabid dog; one died same night; other showed no evidences of injury and examination of brain was negative six months later. The following day, a third pig was inoculated with emulsion from this same dog; no

evidences of injury and "careful examination of many sections of both hippocampus major and cerebellum gave a negative result" 13 months later. Several instances cited, showing uncertainty in reaction of guinea-pigs to glanders infection. "Aside from these cases, we have several times failed to get a reaction in the pigs when the potato cultures from the swabs showed typical colonies and these injected into pigs proved to be B. mallei."

Doubtless, numerous investigations have been carried out to show that guinea-pigs do not vary in their resistance to digitalis intoxication, but I have been unable to find the report of a single series of experiments performed with the object of showing that guinea-pigs are not fully as much influenced by adventitious circumstances as are frogs. On the other hand, Houghton [12] states that he found guinea-pigs unsatisfactory as compared to frogs and Gley [9] mentions variability of the animals depending upon weight, and, as most important cause, the "physiologic factor," the degree of organic resistance, due to individual peculiarities. In view of these statements and the rather suggestive results of Arms, it would seem advisable to make such a report before advocating the use of guinea-pigs to the exclusion of other animals.

The Philadelphia committee [17] state that Edmunds and Hale found that only three-fourths of the dose necessary to cause systolic stoppage of the frog's heart within an hour was needed to kill the animal in 12 hours. In the bulletin containing the report of Edmunds and Hale,[5] the results secured by each of the frog methods is summarized. Comparing these results in tabular form, we have:

	M.L.D. in 12 hours.		1 hour method.	
Preparation	cc	mgms.	cc	mgms.
B. W. & Co.	0.015	1.5	0.020	2.0
Mulford No. 2	0.020	2.0	0.016	1.6
S. & D.	0.027	2.7	0.027	2.7
P. D. & Co.	0.029	2.9	0.021	2.1

It is seen that only in one instance was the dose determined by the 12-hour method smaller than that determined by the one-hour method. I shall endeavor to point out later that these methods *are not similar* and we should not expect the same results. One advantage possessed by the one-hour method is that the lymph sac is opened preparatory to exposing the heart and any unabsorbed drug is discovered, enabling us to disregard that animal, an ad-

vantage certainly not possessed by the guinea method, for Nestor [14] has shown that with rabbits, digitalis injected subcutaneously often becomes encysted and is not absorbed. Focke [7] is convinced, from many control experiments, that the question of absorption does not influence the results secured by the use of his method, in which the end is reached in from 8½ to 10 minutes.

The statements that digitalis always kills mammals by its action on the heart is not generally admitted. Edmunds and Hale [5] say: "On both mice and guinea-pigs, however, the cause of death in probably every case is not due to an action upon the heart, but upon the medulla. In every animal we examined we found the heart beating after the respiration had stopped and it *continued to beat as long as artificial respiration was maintained.*" Cushny [3] also states: "This stimulation, like that of picrotoxin, seems almost entirely limited to the medulla oblongata in many cases. . . . These alterations are much greater than those caused by the interruption of the circulation, and are, therefore, independent of the action on the heart to which they have been erroneously ascribed. . . . To the same cause is to be attributed the rapid, deep respiratory movements and convulsions which are often observed in the later stage of poisoning and which are evidently not due to cerebral anæmia, as has been supposed, for the brain at this stage receives quite as much or more blood than it normally does."

In a very thorough investigation carried out upon rabbits, Nestor [14] concludes that death from digitalis poisoning is always due to the action of the drug upon the respiration. He shows that when the symptoms of intoxication are of the most distressing kind, the institution of artificial respiration causes them to disappear. He shows that if a rabbit is given a dose of digitalis of such size that, uninterfered with, it always causes death, this animal can be saved by the maintenance of artificial respiration for several hours. He shows that the amount of digitalis which always kills the intact animal, when added to the liquid circulating through the perfused rabbit's heart, never causes cessation of the cardiac contractions. Finally, he removed the hearts of rabbits dead from digitalis poisoning and saw them commence to beat normally when perfused with Ringer's solution. "D'une façon absolument constante les cœurs reprenient vie et battaient bien. Et ce n'est pas seulement le cœur du lapin qui peut se comporter de la sorte apre's l'intoxication digitalique, mais nous avons répété les experiences avec le cœur *du cobaye,* du rat, et du pigeon."

All lethal dose methods are objectionable, because they offer nothing characteristic. The fact that a given preparation is capable of killing an animal is certainly no proof of its therapeutic value. The active glucosides of digitalis may become decomposed into such bodies as digitalresin and toxiresin, which, resembling picrotoxin, have a depressant action on the heart, and a preparation containing a large amount of such decomposition products, while testing high by lethal dose methods, might not only be below standard, but capable of causing dangerous poisoning. On this account, Houghton's method is open to criticism. Still less satisfactory, however, is the guinea-pig method, for, in addition to being only a lethal dose method, the animal probably always dies from the action of the drug on the central nervous system. As Edmunds and Hale[5] put it, "One solution might be very weak in its action upon the heart and yet contain decomposition products of digitalis whose typical action is upon the medulla, and it would, therefore, appear unduly strong when judged by such a standard. For this reason, we think that methods which employ as a standard the minimum lethal dose upon the higher animals are not applicable to the physiological assay of digitalis series."

It is in this respect that the one-hour and Focke's methods are much superior. In both of these, the condition of the heart is taken as a criterion. That this action on the heart occurs before the death of the animal is shown by the not uncommon observation of frogs able to crawl around and very much alive but whose hearts present the characteristic "digitalis" picture when the thorax is opened; a picture produced by no drug with which I am acquainted except digitalis and its allies. I am convinced that such animals as these would recover from the intoxication produced by digitalis if they were not molested and the point should be emphasized that these "frog heart" (Focke's and the one-hour method) methods *are not lethal dose methods.* Focke's method is rather complicated and the fact that it necessitates opening the thorax of an unpithed frog should prevent its adoption.

That the two "frog heart" methods are accurate within 10 per cent. is admitted. The cost is a feature that must be considered in any commercial method of assay, and a dozen frogs can be purchased for the same amount as one guinea-pig; thereby enabling many more control experiments with frogs for the same monetary expenditure for material.

The final test of any method of drug assay must rest with the clinician. So far as I can learn, no such clinical trial has been made of the guinea-pig method; while Pratt [11] in this country and Focke [7] in Germany, have shown conclusively that the therapeutic value of digitalis leaves runs parallel with the potency as determined by the "frog heart" methods.

In conclusion, we may say:

1. That the variations in the reaction of frogs can be nullified by the use of ouabain as a standard.

2. That it has certainly not been proved that guinea-pigs possess any marked advantages as experimental animals for testing digitalis over frogs.

3. That lethal dose methods are unsafe, while the one-hour frog heart method is both a good qualitative and quantitative test for the heart tonics.

I wish to acknowledge my indebtedness to Dr. J. P. Simonds and Mr. C. R. Eckler for assistance in the collection of data.

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GRANATUM (POMEGRANATE).*

By John Uri Lloyd, Phar.M.

Punica granatum has been found in cultivation from the earliest historical times. It is now found in all warm countries of the world, and frequently as an ornamental plant in this country and abroad, where it requires protection during the winter season, as it will not endure the cold. It is recorded, *e.g.,* that in 1838 the pomegranate trees in the neighborhood of London were killed by the frost. The form generally grown as ornament is the double variety, and consequently barren. The fruit of the pomegranate

* Bulletin No. 18, Pharmacy Series, No. 4, will give a brief history of every vegetable drug of the Pharmacopœia of the United States, 1900 edition. This, like other Lloyd Library publications, is not in general circulation, being designed solely for exchanging for the publications of Societies and Academies of Science Extra copies will be printed for those who, before May 15, enclose one dollar to "The Lloyd Library," Cincinnati, Ohio.

has been esteemed a delicacy from the most ancient time, and we often see it offered for sale at our fruit stands. In the West Indies, where the plant would thrive naturally, it is not extensively cultivated, and the writer of this botanical history (C. G. Lloyd), who has visited all these islands, does not remember to have seen it or its fruit here. Like all cultivated plants, it is liable to variation, and several of its forms have been considered distinct species and named by several authors; however, they are all now considered forms of one species.

The pomegranate shrub, according to De Candolle, is originally a native of Persia and adjacent countries, but has been cultivated and naturalized in the Mediterranean countries, at such an early date that it has even been considered indigenous to these countries.

Pomegranate was included among the vegetables that were held sacred by the Assyrians and the Egyptians. The latter nation made it a custom to place in the graves of the dead fruits of the field and garden, among them pomegranates, specimens of which are preserved to the present day. The pomegranate had undoubtedly an occult significance with the ancient nations. It was frequently used as a mystical emblem in adorning the capitals of Assyrian and Egyptian columns, and the Bible (1st Book of Kings, vii, 18, 20) tells us that in the building of Solomon's Temple the capitals of the columns were decorated with a "network of pomegranates." Also (Exodus, xxviii, 33, 34), the hem of the high priest's robe was adorned with imitations of pomegranates in blue, purple and scarlet, alternating with bells of gold. The pomegranate was one of the three fruits brought to Moses by the men that he sent to spy out the land of promise. Many other passages scattered throughout the Bible refer to our plant, and testify to the esteem in which the tree and the fruit (then called rimmon) were held in ancient times. The fruit and seed of the pomegranates are often mentioned in the "Arabian Nights."

Pomegranates were represented on Carthaginian and Phenician medals and on the reverse of the coins of the Island of Rhodes. In Greek mythology the pomegranate is very conspicuous and symbolizes fecundity and abundance. The fruit was dedicated to Juno, a deity always represented in sculpture as holding a pomegranate.

The Greek authors, *e.g.*, Theophrastus, describe the pomegranate under the names of "roa" and "roa side"; also Dioscorides, who quite explicitly sets forth the medicinal properties of

the different parts of the plant. Among Roman authors who describe the pomegranate and its uses are Cato Censorius, Pliny, Celsus and others. Subsequent writers, for example, the Arabians, in the ninth century, also refer to the pomegranate, but seem to have mainly reiterated the substance of the writings of their Greek and Roman predecessors. The "Arabian Nights" speaks of the use of the seed cooked as follows: "Every day I cook, five dishes for dinner, and the like for supper; and yesterday they sought of me a sixth dish, *yellow rice,* and a seventh, a mess of *cooked pomegranate seed."* (Adventures of Mercury Ali of Cairo, vol. vii, p. 185..) Of the writers of the Middle Ages, may be mentioned Tragus and J. Bauhinus, the latter giving a most detailed compilation of that which was known before his time on the subject of the pomegranate, including the myths with which it is connected. It was not until the present century, however, that the literature of the pomegranate was enriched by the study of its chemical aspects.

PETROX PREPARATIONS.

By George M. Beringer, Ph.M., and George M. Beringer, Jr., P.D.

Since the introduction of Oleic Acid and the Oleates to medical practice by Prof. John Marshall of London in 1872, much has been learned concerning the action and use and the proper forms for the application of such medications.

Following his effort, a number of valuable papers were contributed to the medical and pharmaceutical journals. In the main, these dealt with the chemistry and were directed toward improving the methods of preparing the oleates of the alkali and metallic bases used in medicine so as to obtain more permanent and definite chemical compounds of a character suitable for use in ointments or in some cases as dusting powders. Yet in these forms, the remarkable penetration and absorbability possessed by Oleic Acid that makes it so valuable as a carrier for many medications, was but very poorly exhibited or utilized.

True, the so-called oleates of the alkaloids were simultaneously developed. These solutions of alkaloids in oleic acid contain a large excess of the solvent that is not needed for chemical reasons nor is it desirable for therapeutic activity. Very little attempt has

been made to make this class satisfactory and pleasant and the disagreeable rancidity of the oleic acid in such excess has no doubt deterred physicians from prescribing them, and statistics, as well as our personal experience, show that despite official recognition of a number of these oleates, their use is exceedingly rare.

Subsequent investigations proved that it was not necessary to use oleic acid in full strength as a vehicle for medication. Also that absorbability of oleic acid is really increased when it is more or less saponified by ammonia. Further that such an ammoniacal soap was miscible with fixed oils, notably paraffin oil, to produce a basic preparation which possessed most valuable properties and as a medium promised most extensive application.

It forms with water an emulsion, and when in practice it is rubbed into the surface it penetrates the pores of the skin and emulsionizes with the moisture and secretion present in the tissues and thus becomes even more rapidly absorbed and distributed than is pure oleic acid.

This basic preparation, which we call petrox, is an excellent solvent for many of the substances applicable externally as remedial agents in inflammations, congestions, rheumatic or other pains, skin affections, etc. Its solvent and penetrating properties certainly make it a most valuable vehicle and medium for topical medications.

Certain of the medicated forms, such as the iodine, methyl salicylate, guaiacol and creosote petrox preparations have also been recommended for internal administration in gelatin capsules or in suspension in milk or wine or other diluent.

While the names of eminent specialists have been associated with the introduction and endorsement of many of the medicated forms of petrox, their extensive use is no doubt largely due to the commercial exploitations of certain pharmaceutical manufacturers. These manufacturers have commonly adopted proprietary titles for their products and it is to be regretted that some should attempt to becloud the real composition and formula by the introduction of such vagaries and misleading statements in their literature as "an oxygenated hydrocarbon," "partly oxydized hydrocarbon" and that the "solid form," recommended as an ointment base, is an "inspissated form of the liquid."

The British Pharmaceutical Codex and the Ergänzungsbuch zum Deutschen Arzneibuch each contain a series of formulas for this class of preparations. The latter uses as a title "Vasolimentum,"

and the Codex "Parogenum," and as English synonyms Parogen, Vasoliment and "Oxygenated Paraffin," thus perpetuating one of the vagaries of the proprietary medicine man's advertisement.

The present edition of the National Formulary contains only formulas for the two basic preparations, "Liquid Petrox" and "Solid Petrox," but it is proposed to introduce in the forthcoming revision a full line of such formulas. This contribution to the subject is the result of an extensive series of experiments that we have carried out in order to determine proper formulas therefor. Most of the details of such experimentation and the failures are omitted and only formulas tried and in our opinion satisfactory are here presented.

Neither the official nor the sub-titles should be unwieldy, but should be such as are euphonious and to become popular should lend themselves to the customary abbreviations of prescription writing. The present N. F. Latin titles, "Petrolatum Saponatum Liquidum" and "Petrolatum Saponatum Spissum," are too long and cannot be readily abbreviated; and these objections become more pronounced when added to a specific name, as in the compound preparations. Such could never be popularized and would detract from the use and usefulness of the formulas.

The present N. F. has adopted as popular English title "Petrox," which precedes the British Codex title in publication and is already to some extent established in practice and must be retained at least as a popular title. It moreover lends itself easily to combined names for the compounds and it can likewise be readily Latinized into forms which are fairly euphonious.

This class of preparations is distinctly different from all other official classes and is of sufficient importance to warrant the adoption of a distinguishing title. This leads to the suggestion that we adopt in the revision of the N. F. as the Latin title PETROXOLINUM and synonyms Petroxolin and Petrox. In order to demonstrate this point these terms and the compounds thereof are used throughout this paper.

Anyone who has worked with oleates, knows how disagreeable and persistent is the odor of oleic acid. It is surprising that in this entire list of formulas as given in the Br. Ph. Codex and Ergänzungsbuch and likewise as marketed by several manufacturers as proprietaries, there is no attempt to overcome this drawback to their use by the addition of a perfume. The addition of a small

amount of Oil of Lavender largely overcomes this objection and makes a decided improvement in the preparations and is an innovation that we should introduce.

The compound preparations of this class are always listed as containing a definite percentage of the active medicament and for this reason as well as for the practicability of the work and to avoid the soiling of measures, the formulas submitted are all constructed on a percentage basis and the *ingredients are all weighed.* This departure from our established rule of weighing solids and measuring liquids is for reasons quite apparent, preferable in this class.

The N. F. directs the use of Spirit of Ammonia and the Br. Ph. Codex Ammoniated Alcohol 5 per cent. in some formulas and 10 per cent. in others. Spirit of Ammonia is so rarely called for, that it is kept in stock by comparatively few druggists and even when in stock it is usually deteriorated and of uncertain strength. This led to experiments to determine if it could not in these formulas be replaced by ammonia water and alcohol. We found that this was feasible and have framed the formulas accordingly.

Another point that needs emphasis, is, that while the "Liquid Petrox" will answer as the base for some of the medications or compounds, it cannot be used alone as the base for the preparation of many of the important formulas. Such preparations as Iodine Petrox, 10 per cent., and Iodoform Petrox cannot be made by simple solution but the medicament must be incorporated by proper manipulation in the course of preparation. In others, the proportion of oleic acid or other ingredient must be somewhat modified to obtain perfect solution and a satisfactory product.

The methods of manipulation as directed in the formulas, are those that were found necessary and it is quite important that these be carefully followed as deviation or careless manipulation may spoil the product.

PETROXOLINUM LIQUIDUM.

Liquid Petroxolin. Liquid Petrox.

Liquid Petrolatum	50 Gm.
Oleic Acid	28 Gm.
Oil of Lavender Flowers	2 Gm.
Stronger Ammonia Water	5 Gm.
Alcohol	15 Gm.

Mix the Liquid Petrolatum, Oleic Acid and Oil of Lavender Flowers, in a flask, then add the Alcohol and finally the Stronger Ammonia Water and agitate thoroughly until clear, warming the mixture slightly, on a water bath if necessary.

Slight warming may be required in cold weather, to promote the saponification.

A yellowish-brown liquid, soluble in ether, chloroform, benzine and acetone, produces an emulsion on agitation with twice its volume of water.

The proportion of the ingredients in this formula does not vary very greatly from that in the present N. F. formula. The product forms a permanent emulsion with water. The formula of the Br. Ph. Codex yields a preparation that will not even form a good temporary emulsion with water, but separates almost immediately.

PETROXOLINUM CHLOROFORMI CAMPHORATUM.

Camphorated Chloroform Petroxolin.
Camphor and Chloroform Petrox.

Chloroform	25 Gm.
Camphor	25 Gm.
Liquid Petroxolin	50 Gm.

Dissolve the Camphor in the Chloroform, then add the Liquid Petroxolin.

PETROXOLINUM CADINI.

Cade Petroxolin. Cade Petrox.

Oil of Cade	25 Gm.
Liquid Petroxolin	75 Gm.

Mix them.

PETROXOLINUM CRESOTI.

Creosote Petroxolin. Creosote Petrox.

Creosote	20 Gm.
Oleic Acid	5 Gm.
Liquid Petroxolin	75 Gm.

Mix them.

The Br. Ph. Codex directs the creosote formula to be only 5 per cent. creosote, yet calls for 20 per cent. of guaiacol in the formula with the latter medication, but as the manufacturers list

both as 20 per cent. formulas, it was deemed advisable to make our formulas correspond with the usage of American practice. If 5 per cent., however, be adopted, then the addition of Oleic Acid will not be required in this formula.

The Creosote, Guaiacol and Eucalyptol Petroxolins all darken considerably on keeping and if that is deemed to be an objection they can readily be prepared as wanted. The darkening is probably due to traces of iron in oleic acid and is not serious as it cannot affect the medicinal action.

PETROXOLINUM EUCALYPTOLIS.

Eucalyptol Petroxolin. Eucalyptol Petrox.

Eucalyptol .... 20 Gm.
Liquid Petroxolin .... 80 Gm.
Mix them.

PETROXOLINUM GUAIACOLIS.

Guaiacol Petroxolin. Guaiacol Petrox.

Guaiacol .... 20 Gm.
Oleic Acid .... 5 Gm.
Liquid Petroxolin .... 75 Gm.
Mix them.

PETROXOLINUM HYDRARGYRI.

Mercury Petroxolin. Mercury Petrox.

Mercury .... 30 Gm.
Hydrous Wool-Fat......................... 15 Gm.
Solid Petroxolin .... 55 Gm.

Triturate the Mercury with the Hydrous Wool-Fat until it is distributed and globules are no longer visible when examined with a lens magnifying ten diameters; then add the Solid Petroxolin and mix thoroughly.

The percentage of mercury has been reduced to 30 per cent., which in a base so readily absorbed is believed to be ample to produce salivation.

PETROXOLINUM ICHTHYOLIS.

Ichthyol Petroxolin. Ichthyol Petrox.

Ichthyol .... 10 Gm.
Oleic Acid .... 5 Gm.
Liquid Petroxolin .... 85 Gm.
Mix them.

PETROXOLINUM IODI.

Iodine Petroxolin. Iodine Petrox 10 per cent.

Iodine	10 Gm.
Oleic Acid	40 Gm.
Alcohol	20 Gm.
Liquid Petrolatum	23 Gm.
Oil of Lavender Flowers	2 Gm.
Stronger Ammonia Water	5 Gm.

Reduce the Iodine to a coarse powder by triturating in a mortar and transfer it to a suitable flask, add the Alcohol and then the Oleic Acid and agitate the contents of the flask until the Iodine is dissolved; now add the Oil of Lavender Flowers and the Liquid Petrolatum and mix the liquids and finally add the Stronger Water of Ammonia, shaking the mixture until a clear solution results.

It was found impossible to prepare a 10 per cent. Iodine Petrox by simple solution in the liquid Petroxolin. By improper mixing there results another difficulty, namely, the separation out of the iodine as a salt, and this is a difficulty that has not been overcome by some of the manufacturers of the proprietaries. The writers have examined several bottles of one manufacture that is greatly prescribed in which appeared quite heavy crystalline sediments that proved to be ammonium iodide. A sample made by the proposed formula has now been kept for more than five months without sign of any separation of crystalline deposit.

PETROXOLINUM IODI DILUTUM.

Diluted Iodine Petroxolin. Iodine Petrox 5 per cent.

Iodine Petroxolin	50 Gm.
Liquid Petroxolin	50 Gm.

Mix them.

ALTERNATIVE FORMULA.

Iodine in coarse powder	5 Gm.
Liquid Petroxolin	95 Gm.

Dissolve the Iodine by agitation with the Liquid Petroxolin in a stoppered bottle.

An assay process should be provided for the Iodine Petroxolins. The Ergänzungsbuch zum Deutschen Arzneibuch gives a method of assay which should, however, be thoroughly tried by competent chemists before adoption in the N. F.

PETROXOLINUM IODOFORMI.

Iodoform Petroxolin. Iodoform Petrox.

Iodoform	3 Gm.
Acetone	20 Gm.
Oleic Acid	10 Gm.
Eucalyptol	3 Gm.
Liquid Petroxolin	64 Gm.

Dissolve the Iodoform in the Acetone, add the Eucalyptol, Oleic Acid and the Liquid Petroxolin and mix the ingredients.

Despite the statements in the books 3 per cent. of iodoform cannot be dissolved in Liquid Petrox alone; even if heat be used, only a portion will dissolve and this largely crystallizes out on cooling. Consequently, one of the solvents for iodoform must be made use of and for this purpose we selected acetone. The disagreeable odor of iodoform is modified and largely overcome by the combination of eucalyptol and lavender.

PETROXOLINUM MENTHOLIS.

Menthol Petroxolin. Menthol Petrox.

Menthol	5 Gm.
Liquid Petroxolin	95 Gm.

Dissolve the Menthol in the Liquid Petroxolin by agitation.

The Br. Ph. Codex makes this only 2 per cent.; we have followed the trade lists in making it 5 per cent.

PETROXOLINUM METHYLIS SALICYLATIS.

Methyl Salicylate Petroxolin. Methyl Salicylate Petrox.

Methyl Salicylate	20 Gm.
Liquid Petroxolin	80 Gm.

PETROXOLINUM NAPHTHOLIS.

Naphthol Petroxolin. Naphthol Petrox.

Betanaphthol	10 Gm.
Liquid Petroxolin	90 Gm.

Dissolve the Betanaphthol in the Liquid Petroxolin by agitation.

PETROXOLINUM PHENOLIS.

Phenol Petroxolin. Phenol Petrox.

Phenol	5 Gm.
Liquid Petroxolin	95 Gm.

Dissolve the Phenol in the Liquid Petroxolin by agitation in a stoppered bottle.

PETROXOLINUM PICIS.

Tar Petroxolin. Tar Petrox.

Oil of Tar	25 Gm.
Liquid Petroxolin	75 Gm.

Mix them.

Oil of tar makes a clear solution and for this use it is certainly to be preferred to tar. Hence we have thus modified the formula of the foreign formularies which direct tar.

PETROXOLINUM SALICYLATUM.

Salicylated Petroxolin. Salicylated Petrox.

Salicylic Acid	10 Gm.
Oleic Acid	5 Gm.
Liquid Petroxolin	85 Gm.

Dissolve the Salicylic Acid in the Oleic Acid and Liquid Petroxolin.

PETROXOLINUM PHENOLIS CAMPHORATUM.

Camphorated Phenol Petroxolin. Camphorated Phenol Petrox.
Campho-Phenic Petrox.

Phenol	12.5 Gm.
Camphor, in powder	37.5 Gm.
Liquid Petroxolin	50.0 Gm.

Mix the Camphor and Phenol and when the mixture has liquefied add the Liquid Petroxolin and mix thoroughly.

PETROXOLINUM SULPHURIS.

Sulphur Petroxolin. Sulphur Petrox.

Sublimed Sulphur	3 Gm.
Linseed Oil	37 Gm.
Oleic Acid	30 Gm.
Liquid Petroxolin, sufficient quantity to make	100 Gm.

Heat the Sublimed Sulphur and Linseed Oil in a flask, on a sand bath, until the sulphur is dissolved, then allow to cool and add the Oleic Acid and sufficient Liquid Petroxolin to make the product weigh 100 grammes, warming the mixture slightly if necessary to obtain a clear liquid.

A dark brown, thick, oleaginous liquid possessing a very foul odor. By itself it is not apt to be applied to humans in this life, but it can be diluted and serves for the preparation of the succeeding formula.

PETROXOLINUM SULPHURIS COMPOSITUM.

Compound Sulphur Petroxolin. Compound Sulphur Petrox.

Sulphur Petroxolin	10	Gm.
Oil of Cade	10	Gm.
Thymol	.3	Gm.
Eucalyptol	3.	Gm.
Oil of Turpentine	30	Gm.
Liquid Petroxolin, sufficient quantity to make	100	Gm.

Mix the Thymol and Eucalyptol, add the Oils and then the Sulphur Petroxolin and finally sufficient Liquid Petroxolin to make the product weigh 100 Grammes.

PETROXOLINUM TEREBINTHINÆ VENETÆ.

Venice Turpentine Petroxolin. Venice Turpentine Petrox.

Venice Turpentine	20	Gm.
Liquid Petroxolin	80	Gm.

Mix them.

PETROXOLINUM SPISSUM.

Solid Petroxolin. Solid Petrox.

Paraffin	37	Gm.
Liquid Petrolatum	20	Gm.
Oleic Acid	30	Gm.
Oil of Lavender Flowers	3	Gm.
Alcohol	5	Gm.
Stronger Ammonia Water	5	Gm.

Melt the Paraffin with the Liquid Petrolatum, on a water bath, add the Oleic Acid, and transfer the mixture at once to a warm mortar; immediately add the Oil of Lavender Flowers and the mixed Alcohol and Stronger Ammonia Water and stir continuously until cool.

This yields a smooth pale-yellow ointment and if the above directions are carefully followed the resulting product is smooth and creamy, very suitable as an ointment base. It is essential that the mortar be warmed so as to insure a gradual cooling and that the stirring be continuous, otherwise the mass will be uneven and granular.

PETROXOLINUM SPISSUM.

THICK OR SOLID PETROXOLIN OR PETROX.

By Otto Raubenheimer.

As this preparation possesses the property of taking up at least twice its weight of aqueous liquids, a point which should be strongly emphasized in the propaganda, I believe it should therefore be of a hard consistency, rather than creamy.

One of the ingredients in this preparation also and again demonstrates the necessity, that, in order to avoid confusion, not only the potent medicaments, but all articles of the same official title in the various pharmacopœias of the world should be identical as to quality, purity and strength.

I refer to Paraffin, which, according to U.S.P., VIII, has a M.P. 51–57° C. and as low as 46° in some commercial samples, but which, according to D.A.B., IV, has a M.P. 74–80°, and which was reduced to 68°–72° in the 5th edition just published.

The U.S.P. product is a petroleum paraffin while the German pharmacopœial product is a refined earth wax or ceresin, entirely different in physical and even chemical characteristics.

As the origin of Vasogen, etc., can be traced to the "Vaterland," therefore the German paraffin or ceresin should undoubtedly be used.

Having made numerous experiments with Solid Petrox, I herewith present three samples together with formulas:

	No. 1.	No. 2.	No. 3.	
Ceresin	30	40	Ung. paraffin 60	Ceresin 4 P. = 24 gm.
Liquid petrolat.	22	20		Wool-fat 1 P. = 6 gm.
Oleic acid	35	27	27	Liq. petrol. 5 P. = 30 gm.
Oil lavend. flow	3	3	3	
Alcohol	5	5	5	
Strong am. wat.	5	5	5	
	100	100	100 gm.	

No. 1 is Beringer's Formula, substituting or better replacing paraffin with ceresin.

In No. 2 I increased ceresin to 40 (from 30) and decreased Oleic Acid to 27 (from 35) and Liquid Petrolatum to 20 (from 22).

Its harder consistency makes it better adapted for use during the hot weather.

In No. 3, I have employed what I consider an ideal hard ointment base, namely Ung. Paraffini or durum of the D. A. B. V. (ceresin 4, liquid petrolatum 5, and wool-fat 1 part).

No special precautions were taken with any of these samples, excepting melting on water-bath of ceresin, liquid petrolatum and oleic acid, the addition of the other ingredients and cooling *without* stirring.

In my opinion the description of Solid Petrox in N. F., IV, should state something like the following:

"A yellowish ointment, capable of absorbing at least two parts of water."

Brooklyn, N. Y., March 19, 1911.

THE GENERAL REQUIREMENTS OF THE GERMAN PHARMACOPŒIA (V)*

By G. A. Menge.

To make exhaustive and critical comment upon all of the general requirements of the new German Pharmacopœia would require more time, and tax your patience to a greater degree, than should be tolerated in a minor detail of your program. Therefore, except for some very general features to which it seems to me your attention should be directed at this time, I shall limit my specific discussion to those general requirements which apply to the determination of melting points, freezing points and boiling points.

You are doubtless familiar with the practice, as applied in the old edition of the German Pharmacopœia, of incorporating in the introductory part more or less specific directions covering general

* Read at the March meeting of the Washington branch of the A.Ph.A.

methods and procedure required in determining physical constants, analytical data, etc., and also specific definitions of general terms used in the body of the book—such as coarse, medium and fine (pieces or powder), room temperature, unweighable residue, soluble and insoluble, etc.

This feature of the old edition has not only been continued but has been extended and improved in the new. The advantage—from several viewpoints—of such a special treatment of general methods, terms and other details, seems to me to be obviously very great, and in principle at least should be adopted in the pending revision of the United States Pharmacopœia.

In this connection it is to be noted that for the sterilization of any substances that may require such treatment, the requirement in both the old and the new editions of the German Pharmacopœia is a very general one, consisting merely in the statement that unless otherwise stated, sterilization is accomplished by the application of heat in accordance with the rules of bacteriological technic, giving due regard to the properties of the substance to be sterilized. Obviously real compliance with such a general requirement necessitates some training in the essential principles of bacteriology as applied to sterilization. It is intended, I believe, that the new United States Pharmacopœia shall include some requirement on sterilization. It is plain that either our requirement must be much more specific than the German—probably impractically so—or the training in pharmaceutical schools and colleges should include at least enough bacteriology to cover such a requirement.

The methods and procedure for the determination of the melting points, freezing points, and boiling points of pharmacopœial substances as prescribed in this new edition, seem to me to represent both progress and retrogression—though the former doubtless predominates. In the attempt to justify this general conclusion, permit me to briefly contrast the old and the new requirements and to offer comment upon certain details:

In both the old and the new editions the melting point requirements, as to methods and procedure described in the introductory chapter, are divided into two parts; the first part applying to all pharmacopœial products except the fats and fatty substances, and the second part to the fats and fatty substances.

In the old edition the requirements for compounds of the first class provide the following details: Dry the sample in a desiccator

over sulphuric acid for 24 hours. Introduce sufficient of the dry sample into a capillary tube of 1 mm. diameter to form a column 2–3 mm. high in the bottom of the tube. Attach the tube so charged to a suitable thermometer and immerse in a bath of sulphuric acid contained in a test tube of 30 mm. diameter. Heat gradually with frequent stirring. That temperature at which the opaque mass becomes a transparent liquid and flows together in transparent drops is regarded as the melting point.

In the corresponding requirements of the new edition, improvement is noted in the following details:

1. Beside the same period and method of drying, the sample is required to be "finely divided"; and as previously noted this degree of fineness is specifically defined in another paragraph.

2. The column of sample in the bottom of the capillary must be 2–3 mm. high when "tapped down."

3. The position of the sample with reference to the bulb of the thermometer is definitely defined.

4. A most important improvement, as I see it, is noted in the matter of heating the bath—against no provision on this detail in the old edition, the new edition provides that from a point 10° below the assumed melting point, the rise in temperature shall be at the rate of 2° per minute.

The period and manner of drying is the same "when not otherwise stated," and the definition of melting point is the same.

The most radical change (and one which in my opinion is a step backward) is found in the method applied. The new method requires apparatus which is a cross between the Roth apparatus and the Graebe apparatus without including the specific advantage of either. It consists of a test tube 15 mm. in diameter and 30 cm. long, containing sulphuric acid to a depth of 5 cm., and adjusted in the neck of a round bottomed bulb of 80–100 cc. capacity having a neck about 20 cm. long, and 3 cm. in diameter, and containing sufficient sulphuric acid to two-thirds fill the neck when the test tube is in place.

The most serious defect in the new method, as I see it, is the absence of stirring, a detail which I consider essential to a well controlled melting point determination, and which is not easily applied with such a double bath apparatus. In this detail, therefore, I feel that the new requirements constitute a definite retrogression as compared with the old.

It seems to me also that in the matter of definition of the melting point the book leaves a large opening for progress toward more rational and adequate pharmacopœial standardization. I am firmly of the opinion that the requirement of a definite *melting interval* or range rather than a *melting point,* would establish a more logical and effective standard.

The old requirements for the fats and fatty substances involve the use of a thin-walled capillary tube of not more than 1 mm. diameter, open at both ends. Enough of the melted fat is drawn into one end of the tube to form a column about 1 cm. high, and is then cooled at 10° for 24 hours to insure complete solidification. Attached to suitable thermometer the sample is immersed in water contained in a test tube of 30 mm. diameter. The bath is gradually warmed with frequent stirring. The temperature at which the fat becomes transparent and rises in the tube is the melting point.

The new requirements differ in the following details:

1. A U-shaped capillary of 0.5–1 mm. diameter, filled with molten fat to the same level in each arm replaces the straight tube.

2. The sample is cooled on ice for 2 hours, or at 10° for 24 hours.

3. The charged tube is attached to a suitable thermometer so that the sample will be on a level with the thermometer bulb.

4. A bath of equal parts of glycerin and water displaces the bath of sulphuric acid.

5. Temperature must be raised "very slowly" to avoid superheating.

6. That temperature at which the fat becomes perfectly clear and transparent is the melting point.

I am of the tentative opinion that the U-capillary is not an improvement over the straight capillary in determining the melting point of fats. This constant is generally more difficult of exact determination as applied to fats than for the other class of compounds. It is claimed by authorities on fats that some fats become clear and transparent before complete melting while others remain cloudy for some time after, and therefore perfect clearness and transparency is not a good criterion of the melting point. For the purpose of pharmacopœial standardization, however, the main thing, it seems to me, is to select some behavior, in the region of the much mooted "true melting point," which is easily observed and reasonably constant. With the old method, the rise of the

fat in the tube under the slight pressure of the water would seem to fulfill such a condition and to indicate at least the melting point of that portion of the fat which is in direct contact with the tube. More extended experience with fats might of course change my views on this point.

The absence of stirring as a requirement in these determinations, although perhaps not so serious an omission as for melting points at higher temperature, still seems to me a mistake.

The requirement in the new edition of a method for the determination of freezing points is all on the credit side—no such requirement being found in the old edition. The method is substantially as follows: Ten grams of the substance under investigation are carefully melted in a test tube containing a suitable thermometer. By dipping the tube in water, the temperature of which is about 5° C. below the freezing point of the substance, the melt is cooled to about 2° below the freezing point; then by stirring with the thermometer, or if necessary by seeding with a small crystal of the substance under investigation, freezing is induced and the highest temperature observed during the freezing process is the freezing point.

The method has the advantage of extreme simplicity, and is therefore readily available to all concerned. It is also probably adequate for the purpose intended, but without personal experience with the method I hesitate to offer critical comment, except perhaps that the dimensions of the test tube, and also of the thermometer, used should be specified. The latter criticism is of general application and will be referred to later.

Just as for the freezing point, the methods described for the determination of the boiling point constitute a feature of the new edition not found in the old, and therefore represent a distinct advance in standardization.

As in the case of the melting point, the boiling point requirements are divided into 2 parts:

The first part describes a method which is intended to serve only as a means of identification of the liquid, and not as a test of its purity. The procedure is somewhat similar to that described for the first melting point method. A thin-walled capillary tube of 3 mm. internal diameter and containing 1–2 drops of the liquid under investigation is attached to a suitable thermometer and immersed in a bath of sulphuric acid just as in the first melting-

point method. A second capillary tube open at the lower end and sealed about 2 mm. above the open end dips into the liquid in the main capillary to prevent bumping. The temperature at which an unbroken series of bubbles begins to rise from the bottom of the liquid is the boiling point.

Having had no experience with this or a similar method I offer no critical comment.

The second boiling point method described is intended to determine the purity of the liquid and of course involves distillation. It is required that at least 50 c.c. of the substance be distilled from a distilling flask of 75–80 c.c. capacity. The bulb of the thermometer must be placed 1 cm. below the delivery tube of the flask. Before beginning distillation a small piece of broken porcelain is placed in the liquid to prevent bumping. The flask is heated in an air bath. *Nearly* the entire liquid must distill over within the required temperature—any low boiling fraction and any residue should be only *very small.*

It seems to me that this method might be improved by being more specific in detail; for instance, the length and diameter of the neck of the flask and the position of the delivery tube with relation to the mouth of the flask should be defined. Also such indefinite phraseology as "*nearly*" and "*very small*" are surely out of place in the *standardization* of a physical constant. It would seem feasible, instead, to incorporate in the description of individual liquids a percentage yield of distillate that should be obtained within the required limits of temperature; or to have a general percentage-yield requirement, applied to all liquids "unless otherwise stated."

Finally: I consider that the general requirements covering melting points, freezing points and boiling points, are seriously deficient in the lack of more specific limitations regarding the thermometer to be used. The book uniformly prescribes the use of "einem geeigneten Thermometer"—a phrase, which I have translated "a suitable thermometer," although possibly it could with equal accuracy be interpreted to mean "an accurate thermometer." In either case, however, my criticism applies, with little variation. Much argument might be offered to justify my attitude on this point—a single illustration I believe will serve the purpose: Of two equally accurate thermometers, standardized in the same way and covering the same range, one might be six inches long and the other three feet long—obviously

direct observations of the same melting point with the two thermometers registering near their upper limits would be widely divergent. I am firmly convinced that if we are to approach real standardization of these physical constants, the pharmacopœial requirements must include either the use of a standardized thermometer with application of correction for emergent stem, or the use of a perfectly uniform standardized thermometer (*i.e.*, an official thermometer). In the latter case the emergent stem correction might be omitted without effect on *standardization*, but with sacrifice of the greatest *accuracy*.

NOTE.—Much more extended and detailed discussion of melting-point requirements, as applied to the United States Pharmacopœia, will be found in Hygienic Laboratory Bulletin 70, of the Public Health and Marine Hospital Service.

PHILADELPHIA COLLEGE OF PHARMACY.

ANNUAL MEETING.

The annual meeting of the College was held March 27th, 1911, at 4 P.M. in the Library. In the absence of President French on account of illness, the First Vice-President, Dr. Richard V. Mattison, presided. Thirty-one members were present. The minutes of the quarterly meeting held December 27th, 1910, were read and approved. The minutes of the Board of Trustees for the meetings held December 6th, 1910, January 3rd and 25th and February 7th, 1911, were read by the Registrar, J. S. Beetem, and approved.

The Annual Report of President French was read by the Secretary and ordered entered on the minutes. The following items of information are abstracted from the Report:

The property as a whole is in good condition. The furnaces and engines have been repaired putting the heat and light plant in first class condition. Improvements have been made in the Pharmaceutical Laboratory, adding materially to the convenience of the teaching force and to that of the Students, and greatly facilitating the increased work of the department. The ceiling between the fifth floor and attic of the Tenth Street building was torn out so as to convert the room into a Gymnasium, giving splendid ventilation and enabling the Board of Trustees to establish a high grade Modern Gymnasium. The alterations in the Pharmaceutical Laboratory and the establishment of a Gymnasium cost $2166.72.

The department of Physical Training has proven of benefit to the Student body. Many Physical defects existing, especially those of the eyes, ears and throat have been corrected, and the systematic exercises given to the classes has added much to the health and comfort of the Students.

The total number of Students enrolled was 515.

In the Chemical Laboratory ninety-one students are doing individual work, and seventeen, thesis work. There have been twenty-five special chemistry students during the year. Twenty third-year students are doing thesis work in the Pharmaceutical Laboratory. There are twelve students in Bacteriology, and also some carrying on special investigations.

The Department of Botany and Pharmacognosy has made material progress during the year, but unfortunately is much crowded and badly in need of more room to extend their work. One of the most valuable adjuncts is the greenhouse and botanic gardens on the roof of the Annex building. The students derive much benefit from the same. The growing plants are used for class instructions, and are utilized for special investigations. Inquiries from various parts of the country are not infrequent regarding the conditions for growing medicinal plants, and it is gratifying to those in charge to be able to supply this information.

The Pharmaceutical, Chemical and Analytical Laboratories are now over-crowded, the Annex building on Cherry street gave temporary relief, but the growing demands of the classes are now so great that it seems necessary that increased accommodations be secured in the near future. The College location was originally a residential section, but with the lapse of years it is now surrounded by manufacturing establishments which must necessarily imperil the historic Collections in the building. These collections if lost could never be replaced—they possess a world wide reputation, and it is the urgent duty of your organization to preserve them for future generations. With this thought in mind your President has for three years past been endeavoring to secure from the City of Philadelphia a site for a new building, and it is hoped that in the near future this may be secured.

The Treasurer will report a material increase of the balance in bank over last year.

It is now a matter of record that the *College Bulletin* and *Alumni Report* have been merged and the first volume of Number Four was issued February 1911 under the Style of "*Bulletin of the Philadelphia College of Pharmacy and Alumni Report.*"

Two members were elected during the year. Four of our members have died during the past year, namely: Dr. Louis G. Bauer, David W. Ross, David Jamison and Caleb R. Keeney.

The Ninetieth Anniversary of the College occurred on February 23, 1911, at which time hearty congratulations were received from a number of the scientific and educational institutions of the city, and your President wishes to extend to those institutions, their officers and faculty his appreciation of their kindly thought, and also to his fellow officers, Board of Trustees and Faculty for their hearty support and co-operation during the year.

REPORTS OF COMMITTEES.

Committee on Pharmaceutical Meetings.—The meetings have been held regularly, and the programs while not as full as heretofore, have been excellent. Various members presided at the meetings. At the April meeting a most interesting discussion took place on Anti-Narcotic legislation which was participated in by many of the members—it was one of the best attended meetings of the entire series. The May meeting was given over to a symposium by students on their theses. This precedent is a good one, as the papers presented show what the apprentices are capable of doing and that the future of our profession will be taken care of. At the succeeding meetings, among those presenting papers were Dr. E. R. Larned of the University of Buffalo, C. Mahlon Kline, Professor H. C. Wood, Jr., George M. Beringer, Jr., and George M. Beringer.

The November meeting was given over to the memorial exercises in connection with the presentation of a portrait of Dr. Susan Hayhurst, the first woman graduate of the College.

The Committee thinks it is safe to say that every retail pharmacist would have saved much valuable time if he were present to have seen the demonstrations in connection with the papers which were read, and it is to be regretted that more do not appreciate the economy of time that results by attending these meetings and that of other associations where papers are read and discussions held.

Publication Committee. THE AMERICAN JOURNAL OF PHARMACY has been issued regularly during the year. There is an increase in the amount received from subscribers and advertisers, and a decrease in the expenses from last year. The old book with the names and records of subscribers which has been used for fifty years, has been replaced by the modern index system. This book is of considerable historic interest and will be placed in the College Collection with the other historic material.

Colleges, Universities, Libraries, and manufacturing laboratories are being constantly added to our list of subscribers, showing that the subscription list is becoming more stable.

Editor's Report. The matter published in THE AMERICAN JOURNAL OF PHARMACY during the past year may be classified as follows: Fifty-four original and selected articles which may be subdivided as follows: two Chemical, twenty-five Pharmaceutical,

two pharmacognostical, six technical, three on biological standardization and sixteen on miscellaneous subjects, quarterly reviews in progress of Pharmacy; thirty-one book reviews; a symposium on maceration and percolation, eight notes from correspondents, also reports of the United States Pharmacopœial Convention, the annual meeting of the American Pharmaceutical Association, the National Wholesale Druggists Association, the American Conference of Pharmaceutical Faculties, the Tenth International Pharmacopœial Congress, Minutes of the College meetings, Minutes of the Board of Trustees and pharmaceutical meetings, abstracts of special lectures, memorial and obituary notes, abstracts and miscellaneous notes.

The most notable feature of the JOURNAL the past year has been the large number of papers dealing with methods and standards of the United States Pharmacopœia, many of these papers were contributed by the chemists of the U. S. Public Health and Marine Hospital Service. Without enumerating more of these papers it may be said that they are of an unusually high order of merit and will no doubt be widely consulted.

Curator's Report. The question of the *identity* of drugs has become a most important question, because the dealer guarantees the identity of the drugs sold, according to certain standards, or suffer legal penalties if the goods be improperly branded. For this reason it has become essential that specimens of drugs of doubtful identity, either wholly or in part, must be compared with specimens of undoubted genuineness. For this purpose standard specimens of drugs are most necessary, and it may be fairly claimed that the drug collections of the Philadelphia College of Pharmacy are probably the best of their kind in this country. These collections are of undoubted authenticity and are rare and valuable. They are being consulted more and more by the pharmaceutical public and to make them more valuable an endeavor should be made to cover the entire field of vegetable drugs, every genera and species and varieties of plants having medicinal value should be added to the collections. Such a collection would be of immense value for reference not only to retail, wholesale and manufacturing pharmacists, but also to government authorities in their legal prosecutions.

Librarian's Report. The Library Committee has gone to considerable expense for re-organization. Fifteen hundred books have

been stamped and marked with the Library ownership, classified, accessioned and shelf listed.

The collection of Pharmacopœias has been brought up to date. New editions of the German, Austrian, Hungarian, Belgian, Swiss, Swedish, Norwegian, Dutch, Russian, Spanish, Italian and Japanese have been added. Since the first of January five hundred and twenty-eight persons have consulted the Library.

The resignation of William Ogilby from active membership was presented, and accepted with regret.

Professor Kraemer presented an enlarged photograph of the late Doctor Susan Hayhurst (the first woman graduate of the College) which had been donated by Mr. F. Gutekunst. The thanks of the College were tendered the donor.

The Committee on By-Laws was re-appointed: George M. Beringer, Joseph W. England, C. A. Weidemann.

The report of the Committee on Nominations were received and ordered entered and filed.

The election of officers, committees and trustees followed, Messrs. William McIntyre and E. M. Boring being appointed tellers. A ballot being taken the tellers reported the result when the following were declared elected.

President, Howard B. French; First Vice-President, Dr. Richard V. Mattison; Second Vice-President, Joseph L. Lemberger; Corresponding Secretary, Dr. A. W. Miller; Recording Secretary, C. A. Weidemann; Treasurer, Richard M. Shoemaker; Curator, Joseph W. England; Editor, Henry Kraemer; Librarian, Katherine E. Nagle.

Trustees for three years: Joseph P. Remington, C. Carroll Meyer, and C. Stanley French.

Committee on Publication: Samuel P. Sadler, Henry Kraemer, Joseph W. England, Joseph P. Remington, M. I. Wilbert, Miss Florence Yaple and Charles H. LaWall.

Committee on Pharmaceutical Meetings: Henry Kraemer, Joseph P. Remington, C. B. Lowe, W. L. Cliffe and William McIntyre.

President French made the following appointments: Delegates to New Jersey Pharmaceutical Association; George M. Beringer, Henry Kraemer, C. B. Lowe, H. L. Stiles and H. P. Thorn.

Delegates to Pennsylvania Pharmaceutical Association: C. B. Lowe, Joseph P. Remington, F. P. Stroup, William McIntyre,

Jacob M. Baer, William E. Lee, Charles Leedom, E. F. Cook, Samuel C. Henry and Clemmons Parrish.

Committee on Hallberg Memorial: F. P. Stroup, H. K. Mulford, W. L. Cliffe.

C. A. Weidemann, M.D.,
Recording Secretary.

ABSTRACT FROM THE MINUTES OF THE BOARD OF TRUSTEES.

Dec. 6, 1910.—Fourteen members present. Committee on Library reported between six and seven hundred books had been classified, accessioned and shelf-listed. Five books were donated during the month. Committee on Instruction reported that Professor Kraemer had recommended Mr. Armin Kohl Lobeck for the position of Instructor in Botany, his duties to begin on June 1st, 1911. The recommendation of the Committee was approved and Mr. Lobeck elected to fill the position. Committee on Discipline reported that a first-year student had presented a false certificate for entrance. After a thorough investigation, the young man, together with his preceptor, were found guilty, and the student was dismissed and informed that he could never again be admitted as a student in the College. Alumni Committee reported that the subject of amalgamating the "*Bulletin*" with the "*Alumni Report*" had been under consideration by the Board of Directors of the Alumni Association, and as a result of their deliberations, they would recommend a merger of the two publications under certain conditions. After a full discussion by the members of the Board, the Report of the Committee was adopted. Committee on Athletics reported that the Gymnasium was completed with an expenditure for total equipment, alterations, etc., much less than had at first been anticipated. Miss Katharine E. Nagle, the Acting Librarian, was elected to active membership in the College. The Dean presented, on behalf of Mr. H. L. Tomkinson, an interesting document in the shape of a bill for professional services by Doctor Lloyd Zachary, covering a period from October, 1746, to November, 1753, and, on motion, a vote of thanks was tendered the donor.

Jan. 3, 1911.—Committee on Library reported that one thousand books had been accessioned and shelf-listed since October, 1910. Several foreign Pharmacopœias recently issued have been purchased and others ordered to bring our collection of Pharmacopœias up to date. Mr. England, for the Committee on Resolutions in

memory of Professor Hallberg, submitted and read same, which were unanimously adopted and an engrossed copy ordered to be sent to the family.

Feb. 7, 1911.—Sixteen members present. Committee on Library reported three hundred and eighty-seven books accessioned since last report. During the past month a number of books were donated. Eighty-one persons had consulted the Library during the month. Committee on Examinations reported that J. Harry Swain had successfully passed his examinations of "Proficiency in Chemistry," when, on motion, it was ordered that the Certificate be granted. Committee on Announcement reported the merger of the *Bulletin* and the *Alumni Report.* The new issue will be published bi-monthly and will contain no advertisements, but will have matters of interest to the graduates and students of the College. It will be sent to all the graduates of the College without charge. Upon invitation, the Board took a recess and visited the Gymnasium to witness a drill by one of the class sections. The president stated that on the 23d of February, 1911, ninety years have elapsed since the founding of the College, and it was his pleasure to extend to the Board of Trustees, the Faculty and the Instructors of the College, an invitation to take dinner in celebration of the anniversary, with him at the Union League, on the evening of February 23, 1911. The invitation was accepted and a vote of thanks extended to Mr. French. A letter was received from Mr. Walter E. Martz, Executor of the Will of the late George W. Hayes, reciting a clause in the Will of Mr. Hayes as follows: "I direct that my gold watch be given to the graduate in chemistry and pharmacy of the Philadelphia College of Pharmacy, who is truly worthy, and who graduates with the highest honors from the said institution, after my departure." Mr. Hayes received this watch as a prize from the College in 1880. It was moved that Mr. Martz be notified that the College would accept the gift and award the same in accordance with the Will. By resolution of the Board, it was directed that an inventory of the Fixtures, Contents, etc., of the College, be taken as would be useful in the event of loss by fire. After a general discussion, it was decided that the heads of Departments and their assistants be requested to begin at their earliest convenience to make such an inventory.

C. A. Weidemann, M.D.,
Recording Secretary.

PRESENTATION OF PORTRAIT OF THE PRESIDENT, HOWARD B. FRENCH, PH. G.

Seldom has the writer had the privilege to be present on such a felicitous occasion as Tuesday evening, April 4, 1911, at the Union League, when a most excellent life-size oil portrait of President French was presented to the College on behalf of the officers, faculty, members of the Board of Trustees, members of the College and Alumni Association. The occasion was one of the great events in the history of the College, and was commemorated by a dinner, which was participated in by not only many of those who had contributed to the fund, but by the Mayor of Philadelphia, the State Superintendent of Education and other officials.

The portrait of President French is of him in his academic gown with cap in hand and was painted by Mr. Hugh H. Breckenridge, a teacher in the Academy of Fine Arts of Philadelphia, and an artist of high standing, particularly by reason of his excellent work in portraiture. The portrait occupied a central position in the brilliantly lighted banquet hall, which was resplendent with floral and other decorations in which the College and national colors were conspicuous. President French, though suffering from a cold, was present, and remained during the greater part of the ceremonies. The menu contained a four-color reproduction of the portrait and will be treasured as an excellent souvenir of the occasion. The addresses were in the nature of personal tributes to President French for his zealous and efficient labors as a man of affairs, as a leading citizen in the civic life of Philadelphia, and Pennsylvania, and as president of one of the oldest educational institutions in America.

Prof. Joseph P. Remington acted as toast-master. In his opening remarks he alluded to the fact that those assembled had met to do honor to Mr. Howard B. French, President of the Philadelphia College of Pharmacy, who had not only done much for the College of Pharmacy, but for the City of Philadelphia.

The portrait was presented on behalf of the members and alumni by Mr. George M. Beringer, A.M., Ph.M., Chairman of the Committee on President French Portrait, and also Chairman of the Board of Trustees of the College.

PRESENTATION ADDRESS BY MR. BERINGER.

MR. TOASTMASTER, HONORED GUESTS, FRIENDS AND FELLOW ALUMNI:

This is a memorable occasion in the history of the Philadelphia College of Pharmacy. Although she has attained the mature age of 90 years, one will search her records in vain for a similar event, and with the modesty that has always characterized her career she to-day pleads "first offense."

Heretofore, the alumni and members of the College, possibly because of the conservatism inherited from the Quaker founders, have refrained from giving any similar public testimony to the worth and appreciation of the services of any of her many faithful officers, during their existence in the flesh, but have been contented to have them await encomiums and merited recognition in obituary notices and with the rewards of the hereafter. On this occasion we have made a notable and universally approved departure from the time honored traditions and customs of the institution.

Do not think that I am going to use this as a proper premise to deduce the conclusion that institutions, unlike men, do not become infirm and decrepit with advancing years, but are rejuvenated with the decades they have passed. However, I will advance as a correct syllogism, that the Philadelphia College of Pharmacy was founded on broad ethical principles to supply a public need for the specialized and practical instruction of those entrusted with the protection of the public in the art of preparing drugs and compounding medicines, and that her officers and faculty have with honor and fidelity always adhered faithfully to the precepts and high ideals of the founders. To these truths we can attribute the success that has made her the model school for pharmaceutical education.

Despite the trying experiences and the greatly added duties and responsibilities that have come with the great strides made in the sciences and in the modern methods of education, she has unfalteringly maintained her principles. With each precept sustained, with each difficulty mastered, with each advance carefully planned and faithfully executed, she has grown stronger and stronger and to-day her renown and her achievements for pharmacy are indelibly stamped upon history and every citizen of this commonwealth should be proud of her standing and jealous of her success

and future prosperity in wider fields of usefulness and research.

Surely she has fulfilled the prediction made by that eminent scholar, medical teacher, and author, Dr. Geo. B. Wood, "that the Philadelphia College of Pharmacy would render the City of Philadelphia the centre of pharmaceutical education."

The success that has attended the College is undoubtedly very largely due to the exemplary men who have been elected as officers. The presidency has always been filled by men of marked ability and sterling character and broad experience who have been prominent in public affairs and assumed a full share of the duties and responsibilities of useful citizenship. Eight gentlemen have been elected as the chief executive since the founding of the College in 1821.

But I must not forget the admonitions both spoken and implied by the chairman of the committee in charge of this public function. First. He wanted me to limit my speech to two minutes for fear of tiring the audience. I crave your indulgence just a while longer even if I do exceed his time limit. Second. I was to refrain from poetical effusion. No fear of driving you away in this manner, the muse is sleeping, if not dead. Third. I was not to attempt oratorical flights. He possibly did not realise what a dead weight I am in this respect as I have never been accused by any one of being an orator. But this was not the reason he assigned. He intimated that the orators would follow and that the pyrotechnical display would be the finale. Again I was not to delve into historical reminiscences, but I cannot refrain from straying from his straight and narrow injunction and reminiscencing just a little.

The first president was Charles Marshall, of whom it has been said "that few nobler men ever lived."

The second was William Lehman, a scholarly pharmacist and legislator who for fifteen consecutive years was elected to the Pennsylvania Legislature and whose name was associated with many of the internal improvements of the State.

The third was Daniel B. Smith, who served as president for twenty-five years. He was a happy combination of business man, philanthropist, literary and scientific scholar, teacher, editor, and author. A man remarkable for the versatility of his attainments and who was associated actively with most of the scientific and charitable organizations then existing in the city.

The fourth was Charles Ellis, who succeeded to the business of his preceptor, Charles Marshall, and whose name for several generations was well and favorably known in the wholesale drug business of the city.

The fifth was Dillwyn Parrish a calm and dignified friend noted for his excellent judgment and wise discretion.

The sixth was Charles Bullock another man of attainments who devoted a large portion of his life to the development of the Franklin Institute and of this College.

The seventh was that "Grand Old Man" William Jenks whose conviction and love for his Alma Mater caused him to immediately resign the honor and duties of the office so that a younger man of energy and aggression might be elected.

The eighth is our present President, Mr. Howard B. French, whom we are pleased to have with us on this occasion as our honored guest and likewise to have on dual exhibition in this life like reproduction, a magnificent example of the art of the artist.

Since 1872, Mr. Howard B. French has been officially connected with the College as a trustee and since 1900, as our President. Without detracting an iota from the veneration and esteem in which we hold the memory of his predecessors in this office we can truthfully say that he combines in his personality most of the good qualities of all of them.

In spite of his large commercial and financial interests, despite the demands of the public, he has always managed to give close attention to the needs of the Philadelphia College of Pharmacy. You who know Mr. French know that he is a most strenuous worker, whose determination, zeal and energy combined with his executive ability enables him to accomplish a vast amount of work. He is one of the progressive spirits who are planning, not for the present day and generation, but whose wise forethought will make the progress of future generations a possibility and conservative old Philadelphia a model modern city and the best of the large cities in the world.

His love for the College, his devotion to her interests, his unselfish and indefatigable labors in her behalf, his indomitable courage and energy, his magnetic enthusiasm, the influence of his practical leadership have all been potent factors in determining her progress and setting the pace for future advancements.

These are but some of the traits exhibited in his official activities

and coupled with a personality, characterized by high ideals and virtues, have endeared our President to the members and alumni of the College.

A short time ago, some of the members of the College conceived the idea that it was only proper and due that some public recognition should be made of the unselfish labors of our President for the betterment of the College; some testimony given of our regard, esteem and love. A meeting was held to consider the subject and it was decided to appoint a committee to present to the Alumni and members a plan to honor him and at the same time add to the valuable collection of portraits owned by the College, by presenting by popular subscription a portrait in oil of our president.

The response of the Alumni was spontaneous and the committee have been over-joyed at the demonstrations of loyalty and the enthusiastic support that has accompanied the movement. An artist of high reputation was selected and we have before us now his finished commission, the excellent and almost speaking likeness of our honored president.

I esteem it as a great honor to act as the representative of the more than 1200 contributors to this fund, and in their behalf present to the College this portrait. In their behalf, I ask that it be accepted as a slight tribute to the efforts and personal worth of the original, a token of the regard and esteem and love that the Alumni has for our president. Further, this occasion signifies and this gift symbolizes the loyalty of our Alumni who are jealous of the fame and honor of their Alma Mater. An aggressive Alumni who are fully alive to her interests and who are praying that a better location and more ample facilities may soon be at her command, and with enlarged opportunities still greater achievements are confidently promised.

We ask that this portrait be preserved and safeguarded and trust that it may be but another inspiration to the members for the perpetuation of that integrity, sincerity, fidelity and adherence to principles that have always characterized the management of the institution. May the sentiments promulgated with its inception and associated with this movement live for ever. May the portrait as it hangs on the College walls prove a silent, yet effective example worthy of emulation, that shall stimulate the coming generations of students to their highest attainments and maintain the Phila-

delphia College of Pharmacy in the lead of all pharmaceutical education.

The portrait was accepted on behalf of the College by Richard V. Mattison, M.D., First Vice-President of the College.

ADDRESS OF ACCEPTANCE OF PORTRAIT, BY DR. MATTISON.

HONORED PRESIDENT, MR. TOASTMASTER, FELLOW ALUMNI AND FRIENDS:

By virtue of my position as First Vice-President of our College, I am accorded the rare opportunity of accepting upon behalf of our members, this portrait of our friend and fellow-alumnus, MR. HOWARD B. FRENCH, a memento in perpetuity of the love which the associates of our self-denying president have for his ever charming personality.

To voice this affection and high esteem, in which more than twelve hundred of our alumni have joined, is, I take it, the real object of this assemblage gathered to-night about this festive board. But in voicing it what can I say that you do not already know about this man whose thoughtful, clear-sighted, far-reaching and most unusual labor upon behalf of the Philadelphia College of Pharmacy has been and is of such transcendent magnitude that we even now scarcely appreciate the enormous possibilities which have been opened up to us through the untiring devotion of our president to our college interests.

As we, therefore, as his fellow Alumni, unite to do him glorious honor this evening, let us accord him with most joyous acclaim the fulsome praise which his deeds command and, in heartsome tribute to the rugged, manly personality of Mr. Howard B. French, unite with the immortal bard in Hamlet and, but slightly paraphrasing, say, "Here *is* a man that, take him all in all, we shall not look upon his like again"—our President.

RESPONSE BY PRESIDENT FRENCH.

MR. TOASTMASTER AND GENTLEMEN:

My physician positively forbade me saying one word. You have been exceedingly kind. You have honored me beyond, far beyond, my desserts; and I thank you all for having me here with you to-night and for doing honor to the College.

THE ADDRESS OF HON. JOHN E. REYBURN, MAYOR OF PHILADELPHIA.

The address of Mayor Reyburn was in the nature of a tribute to President French's services "as a citizen whose public spirit and unselfish labors have been of the greatest value in his relations to this community."

He said: No man other than he could stand before a Philadelphia audience to-day and claim with less dissent or with more truth that he has performed his whole duty toward this city. He has given up not simply honors, but even days to studious thought and active participation for the advancement of the public welfare. His services were not perfunctory, but enlisted the generous impulses of his nature; and he gave actively the very best thought and the most strenuous effort for the good of Philadelphia. I stand here to-night to acknowledge before this assemblage the obligations I am under personally to Mr. French for his strong common sense and for that equipoise of character which made his counsel and co-operation so valuable. There was with him a sort of holding things level, as you know a square man always does; and you can tell instinctively when a man is square. He has that conservative characteristic which I might call a holding back; and yet there was a strength and a fervor in his holding back. It was a powerful influence in itself; and I always recognized him as a safe guide and a reliable counsellor."

His Honor, the Mayor, further said: "To be the head of a great school like that of the Philadelphia College of Pharmacy, which for ninety years has proven its worth in our community, is in itself an honor of which any man might be proud. It is really a great distinction. We know how Mr. French has carried on the work of this institution—not carried it on in the sense of supporting it with money or with great gifts and all that, but by his personal, every day interests in its management, in the welfare of its students and in all that springs from an institution of this kind and that makes it efficient and a benefit to the community in which it is located. As its head, its director and its guide, he has kept the College in the exalted position which it occupies to-day and has occupied in all the years of its useful existence. There can be no question that it is to have a more extended sphere of activity. Indeed, in the logic of events, it cannot fail to share

in the great development that is sure to come to our community and to the whole world in the next generation. Its mission will be ever onward and upward.

"Now this institution deserves to be and ultimately will be placed in a location commensurate with its merit and importance. The example it has furnished, the influence it has wielded, and the great things it has accomplished for the good of humanity, not only in the city and State but in the United States, and I might say, throughout the whole world, entitle it to proper recognition, with the men who have been connected with it, the College has stood out among these institutions of learning, of art and of science, which have made Philadelphia famous."

Continuing, the Mayor said: "As I have said, we want to see the Philadelphia College of Pharmacy where it should be—we might as well say it frankly—upon the Parkway. And if there is anything that I can do to aid in placing it there it will be done. The College should be in a commanding place, where it may be seen by everybody, that the world may know of the good it is doing and will do."

ADDRESS BY NATHAN C. SCHAEFFER, PH.D., LL.D., STATE SUPERINTENDENT OF PUBLIC INSTRUCTION.

Dr. Schaeffer, among other things, said:

"When I was a boy, studying history, I noticed that there were certain names on the pages of that history that had the surname 'great' attached to them; and I asked myself 'What is it that makes the man great?' I noticed that there were only two classes of men in history to whom that surname 'great' was given; the one class being composed of men who had been eminent in the State; men like Charles the Great, Frederick the Great, and Alexander the Great. There was another class of men surnamed 'great' who had been eminent in the church, men like Leo the Great and Gregory the Great. And my perplexity grew when I asked, 'Why is it that men in past ages have only achieved greatness in two lines of human activity, the Church and the State." Well, in my boyish eyes the greatest man in the community was the one who could draw the biggest check and have it honored at the bank; but I very soon discovered that wealth does not make men great on the pages of history. You never read of Rothschilds who were great. Away back in the days when Virgil

wrote and Cicero spoke there were men so rich that they dissolved pearls in goblets of wine to make the drink more costly. But if your life depended upon it, I venture to say, not one of you could mention a single one of those rich men's names. In spite of their wealth their memories have been buried in oblivion. Wealth does not make men great. A man may be a manufacturer and pile up profits so that they will fill the vaults of a bank, but that does not make a man great. I got the notion that it was scholarship that made men great, for I found that on Commencement Day prizes and honors were awarded on the basis of scholarships. But when I began to study the life of Frederick the Great I found in it nothing of scholarship to boast of. He never learned to read his native German with any sort of fluency. Voltaire used to say, in the morning, 'Now I must go and wash the King's dirty linen,' meaning thereby that he must go and correct the King's French. Frederick never could read French accurately, and yet he was great. Scholarship never makes a man great. A man may be the President of a College, and noted for his scholarship, and yet never achieve greatness.

Is it political position? Well, many men have held political positions and they have sunk into oblivion. It is not political position either that helps to give a man his place amongst his fellowmen. Schleiermacher, in his essay on Frederick the Great, says 'that men are great in the degree and to the extent that they exert a moulding influence over their fellow men and render to them helpful service.' In past ages the Church and the State were the only channels through which the sons of genius could reach the masses of their fellow men and thus leave their own age and their own people better than they found them. But the nineteenth century opened up a new channel through which a man can reach his fellow men, and that channel is the school.

The man whom we admire and whom we have gathered to-night to honor has impressed himself upon the community through the school to whose board of trustees he has belonged for many years and at the head of which he has stood during a number of years. This Philadelphia College of Pharmacy has made itself felt not only in Pennsylvania, but even in the far-off countries of Asia and of other lands; and probably it has done more for humanity than some of us are able to perceive.

In the days of John Calvin of Geneva the average length of

life was twenty-one years. To-day, in some of the States of this Union, the average length of life is more than forty years. Is not that partly due to the fact that the druggist has learned how to compound prescriptions for people who are sick, how to administer medicine so that his drugs may not be harmful but their use may redound to the health and the welfare of the people?

No one can deny that our colleges of pharmacy have done very much to add to human longevity. For that reason a college like the Philadelphia College of Pharmacy, which, if my educational history is all right, was not only a pioneer, but the first institution of its kind on the face of the earth, deserves an amount of recognition, in the history of education, that cannot be accorded to an ordinary school. Is it not a pioneer, is it not a forerunner, is it not the parent of a great many schools that are now efficient agencies in curing disease and in lengthening human life?

Max Mueller says that every public man leads three lives while but one life is seen by the people at large. That is the man's public life. Another life is seen only by the man's intimates, by his wife and by those who live with him under the same roof. That is the man's private life. I have always felt that a man deserves great praise when his private life is in strict accord with his public life. And it is for that reason that we are constrained to praise the President of the Philadelphia College of Pharmacy. What is the third life that every man in public life leads? The third life is the inner life, visible only to the man himself and to his Maker on high. When a man's inner life corresponds with his private life and his public life, then we have a model man; the private life and the public life of the man being but an expression of that inner life which is visible only to the man himself and to his Maker. From all that I have been able to learn of the gentleman whose picture is before us, these three types of life have been in harmony throughout his long career.

Now, one word more and I am done. I have had my dreams; and when I visited the College of Pharmacy and saw how every inch of space had been utilized I could not help wishing for that contemplated boulevard with plenty of ground and the requisite facilities to accommodate this institution. Philadelphia is the centre of medical, dental and pharmaceutical education. When I was in the Berlin University, if a man was a Philadelphia dentist he had plenty of practice. Our University here draws a hundred more

students from foreign countries than Yale or Harvard or any university on the Atlantic Coast. This College of Pharmacy draws students from Asia and other foreign lands. It is renowned, both at home and abroad, for the thorough education which it gives. And my wish to-night is that the College of Pharmacy may grow and flourish and that its present President may live long to carry out the plans for its prosperity that he is cherishing. It is also my wish that the official life of our Mayor may be prolonged so that that "Beautiful Philadelphia" shall come when these gray heads can see it and that when that "Philadelphia Beautiful" shall be realized one of the ornaments to which the visitor may point with pride will be the new building, on the Boulevard, of the Philadelphia College of Pharmacy.

ADDRESS BY EDWARD JAMES CATTELL, ESQ., OF THE BUREAU OF STATISTICS OF PHILADELPHIA.

Mr. Cattell, who was introduced by the Toastmaster "as the silver-tongued orator of Philadelphia" made an address which alternated with flashes of humor and eloquence. He said in part:

It seems to me, gentlemen of Philadelphia, that the occasion of the presentation of this portrait, the fact that we are here honoring this gentleman who stands for a type of man good to the core because he wants to be good, not because he has no opportunity to do evil, testifies the highest type of public spirit and is full of promise for the city we all love.

Now, to speak the whole truth—I love Mr. French. I have known him these many, many years. And as I looked upon him to-night, there came back to me an old memory of fifty years ago when, early in the morning of a day in Spring, I first caught sight of his beautiful home in New Jersey. It was a building of snowy whiteness, with strong and beautiful lines rising with a dignity all its own, out of a grove of trees. Something about it was typical of that purity of life which the American home stands for everywhere. As I looked at Mr. French to-night, under his crown of silver,—God-given token of duty well done,—it seemed to me that: in his character, in his life record, in all that he has done for this city that I love, I could see the same strong, clean lines, the same untarnished purity, that stood out so gloriously in the morning sunlight when I first beheld the dear old home in which he learned from mother and father those noble principles

and generous impulses which have always distinguished him. I have at home a bank check drawn by his father—one of the finest men I ever met—to my father, sixty-five years ago. Our parents respected and trusted each other. I respect and love your President and am proud to tender this tribute to his worth and give this public recognition of what he has done for this city.

REMARKS BY HON. ISAAC JOHNSON, STATE BOARD OF CHARITIES OF PENNSYLVANIA.

Mr. Toastmaster and Friends of Howard B. French:

Surely no request from Mr. French to myself to say a word on an occasion like this could be denied, even though I only expressed my honor of being called upon. I thank you for the compliment you have paid this man here to-night. I have known Mr. French a number of years in connection with the State Board of Public Charities. What you have said about him to-night as he is known in the ordinary walks and avenues of life meets a warm response in the heart of every man who has met him in this great work. We do not meet often enough to speak to each other, during our lives, of the work in which we are engaged; as a rule we wait until our co-workers are dead, and then we build monuments to their memory when these cannot do them any good.

It was a great pleasure for me to come to-night to this dinner, to be present at the presentation of this portrait to the School of Pharmacy and to hear the kind words spoken of this man and to him when he can hear them and appreciate them. It is a very great pleasure to be told by those who have known him longest and best that, as he has travelled upon this stream of life until now getting into the way of being called an old man, he has never thrown any mud, was never indiscreet and that he has lived in a city that is cleaner and better for his living in it. What compliment can be paid a man equal to this? The distinguished educator who spoke here to-night pictured to us the wealthy and the educated; and he has told us that it is not wealth or education that makes men great. No; it is a man who picks a fellow up from the roadside and helps him over the rough places of life; it is a man who goes through life, strewing it with blessings—he is the great man. And only he will history perpetuate the memory of.

ADJOURNMENT.

The ceremonies closed at 11.20 P.M. with a round of cheers for President French, in which the entire company, under the lead of the Toastmaster, joined with great enthusiasm.

NAMES OF SUBSCRIBERS TO PRESIDENT FRENCH PORTRAIT FUND.

The collection of the subscriptions was placed in the hands of a special sub-committee, of which Mr. C. Mahlon Kline was the chairman. The replies received, with the subscriptions, showed not only the high esteem which the alumni have for President French and their appreciation of his devotion to the college, but uniformly expressed the affection of the alumni for the college and their desire to assist in every way in advancing her interests and in aiding her in retaining the leadership she now holds.

One of the most pleasing letters received as showing the loyalty of the alumni was that from the widow of a deceased alumnus, who in sending her contribution in memory of her husband added, "it would please him to know that I could help his Alma Mater in so small a way." As the chairman of the Finance Committee has said, "the generous responses of so many of the alumni show that they have the welfare of the college at heart, and these sentiments are really more important to the institution than the donations themselves." It was soon apparent after the Committee got to work that this movement to honor President French had become a movement for welding the alumni together into a coherent and efficient organization and was indeed stimulating not only to the members of the Committee but to all those engaged in the college work.

The following is a list of names of the members of the College and alumni who subscribed to the President French Portrait Fund, the total number being something over one thousand:

Gus G. Anderson, S. D. Addis, F. J. Althouse, Joseph C. Andrews, F. C .Albright, W. E. Allen, H. P. Arnold, John Ayres, H. V. Arny, Robt. B. Anawalt, Robt. W. Allen, Louis K. Acker, Frank I. Adams, E. F. Allen, J. K. Auginbaugh, William Appmann, M. D. Allen, Franklin M. Apple, William H. Andrews, Milton S. Apple, Howard Albert, James D. Adams, James A. Allen, Charles Franklin Adams, William C. Aughenbaugh, Paul Anspach.

Russel T. Blackwood, George B. Beakey, John D. Burg, Maxwell

M. Becker, George Blinkhorn, Grace Lu Babb-Abbott, Charles H. Baldwin, Warren B. Beckler, J. S. Beetem, J. O. Burge, Howard H. Boltz, S. A. E. Brallier, Thomas L. Buckman Charles A. Bye, Isaac A. Braddock, James Stanley Breen, Peter Bienkouski, Helen R. Burns, R. H. Brennecke, S. J. Bannan, John J. Bridgeman C. W. Baas, Russell G. Bush, George H. Borrowes, John H. Booth, Jacob M. Baer, Henry C. Blair, George M. Beringer, Howard J. Baer, Irwin A. Becker, Chas. M. Butcher, Mitchell Bernstein, Chas. J. Biddle, Fred W. Branin, W. C. Bauer, Geo. M. Beringer, Jr., W. E. Brown, H. A. Burkhart, D. A. Buehler, Jesse N. Blalock, C. H. Bernhard, Chas. H. Butters, Henry Blithe, Lulu Brookes, Virginia Brookes, Oliver G. Billings, B. Henry Balle, Albert E. Brown, Willis E. Bowen, Alexander Bachmann, W. C. Burchfield, Chas. B. Baumgartner, H. O. Baer, Samuel Bartholomew, S. J. Banman, Wm. H. S. Bateman, Jennie Block, Wesley J. Barrett, Edwin M. Boring, Ray P. Brown, Edw. H. Buehler, Fred J. Benner, E. H. Burhl, C. L. Bonta, Chas. W. Baas, Edgar Breneiser, E. P. Barr, M. W. Britcher, Geo. Bille, Elam Brubaker, E. F. C. Beecham, J. W. Beckwith, James Buckman, Robert W. Beck, John P. Bates, Max Barkel, T. H. Boysen, F. A. Butter, W. A. Bright, F. A. Bunting, W. L. Bucher, J. C. Boyer.

E. O. Criswell, Albert Cliffe, L. Corson, J. C. Coscey, Wm. F. Cramer, Jr., P. V. Cooper, C. C. Church, Nathan A. Cozens, Edward B. Clark, Wm. E. Cassell, F. F. Coleman, Katherine Cliffe, Norman H. Cloud, R. B. Claudy, M. Costello, W. G. Culby, C. F. Carter, A. D. Constock, Virgil Coblentz, Theo. Campbell, E. F. Cook, David Costelo, Albert R. Calhoun, Milton Campbell, F. W. Culler, F. H. Cappeau, Geo. J. Coleman, Roy T. Cope, J. W. Cotterel, A. T. Clayton, Clarence H. Campbell, W. A. Clingan, S. Ross Campbell, Geo. H. Colton, Thos. C. Coltman, W. A. Carpenter, J. W. Crumbie, C. R. Carrington, T. F. Crawford, H. V. Crawford, W. R. Calvine, A. D. Cuskaden, H. C. Clapham, H. G. Carter, W. L. Cliffe, H. M. Carey, Geo. L. Carman, John E. Carter, Clarence Croft, Jos. Carey, G. J. Crumbis, L. B. Curtis, A. B. Clark, G. F. Crouse, Chas. S. Closson, Lane V. Collins, H. L. Cox, F. W. Cotton, L. B. Coley, John H. Collins, Amanda M. Carslake, Clarence H. Corp, J. K. Challenger, E. D. Chipman, Louis G. Clarke, E. D. Crouse.

H. B. Dilatush, H. J. Darr, Robert L. Dubbs, Walter C. Dugan, L. H. Dielman, R. G. Dunwody, P. R. Donmoyer, W. A. Dorman, H. M. Dorman, W. H. DeBeust, S. B. Davis, L. A. Dresbach, J. H.

Dewees, Kate M. Davidowitch, Henry H. Dancy, Oscar C. Draper, A. Dougherty, J. H. Dewees, Norman R. Dean, Geo. J. Durbin, H. D. Dietrich, C. G. Dodson, Chas. F. Dare, Wm. T. Douglass, H. L. DeKalb, Louis Dielman, John H. Dawson, W. E. Dittmeyer, Guy S. Dunbar, C. A. Duncan, William Dulin, Geo. B. Davis, Harmon Dilks, Jr., Chas. B. Dierolf, W. R. Dawes, Alex. Dubell, C. Wilfred Dare, Howard S. Davis, T. I. Deibert, Servill Douglass, Wm. B. Davis, Edwin A. Donecker, Thos. Donaldson, H. H. Dealeyne, W. R. Decker, Philip C. Dosch, A. J. Ditman, T. S. Deen, John T. Doughty, Chas. W. Dirmitt, C. W. Dare, G. C. Davy, Jos. T. Dougherty, R. B. Dickinson, C. Lewis Diehl, Wm. Drett.

C. P. Eves, Jos. W. Ehman, J. Evans Eckman, Edw. A. Eyer, Chas. W. Eckenroth, J. W. England, Geo. B. Evans, E. G. Eberle, B. H. Eichold, Samuel Evans, Henry Eberhart, H. S. Eckels, T. B. Eisenhart, Evan T. Ellis, D. F. Eft, Horace W. Estlack, M. Bruce Edwards, J. S. D. Eisenhower, Chas. L. Eberle, Wm. Evans, Abner T. Evans, Chas. W. Evans, S. C. Ensminger, Maurice H. Eby, James M. Ebert, Clarence H. Eldon, E. G. Eberhardt, Mrs. Josephine English.

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A. T. Zeller, Chas. S. Zimmerman, H. P. Ziegler.

NAMES OF THOSE PRESENT AT THE TESTIMONIAL DINNER.

In addition to the invitations sent to the members of the College and Alumni, a number of special invitations were sent to those prominent in educational work, and to the presidents of various pharmaceutical associations. While quite a number of the latter responded, a number, however, were unable to attend and sent letters containing their felicitations. These include the following:

Mr. Benjamin T. Fairchild; Prof. E. G. Eberle, President, The American Pharmaceutical Association; Mr. H. B. Guilford, President, National Association of Retail Druggists; Prof. C. Lewis Diehl; Mr. F. Gutekunst; Mr. Samuel W. Fairchild; Governor John K. Tener; Hon. Edwin S. Stuart; Prof. J. W. Holland; Prof. John Uri Lloyd; Dr. William Muir; Hon. J. Hampton Moore; Hon. George D. McCreary; Mr. F. W. Meissner; Prof. H. M. Whelpley; Prof.

William A. Noyes; Mr. George A. Newman; Mr. Frank G. Ryan; Mr. H. B. Rosengarten; Prof. Edgar F. Smith, Provost, University of Pennsylvania; Mr. Harry L. Stiles; Prof. H. C. Wood; Dr. Harvey W. Wiley; Dr. Robt. Ellis Thompson, President, Philadelphia Central High School; Prof. William Trelease; Dr. William J. Schieffelin; Mr. Aubrey H. Weightman, Prof. John J. Abel, President Nicholas, Murray Butler, Dr. N. L. Britton, Samuel M. Clement, Jr., Prof. Charles Caspair, Jr., President A. W. Harris, Prof. Francis E. Lloyd, Hon. Hampton L. Carson, Dr. Samuel G. Dixon, Prof. W. G. Farlow, Dr. Joseph S. Neff and Hon. Wm. Potter. A cablegram was received from Henry S. Wellcome and Dr. Frederick B. Power.

The following list gives the names of subscribers and invited guests that were present at the testimonial dinner at the Union League when the President French portrait was presented to the College:

Jacob M. Baer, Edward F. Beale, W. Ward Beam, Jacob S. Beetem, George M. Beringer, Ralph Blum, John J. Bridgeman, Edwin M. Boring, H. H. Breckenridge, Miers Busch, Hon. Theodore Campbell, T. H. Cappeau, Edward James Cattell, William L. Cliffe, E. Fullerton Cook, Charles F. Dare, L. H. Davis, Hon. Murrell Dobbins, Thomas Donaldson, J. W. Ehman, Joseph W. England, George B. Evans, S. K. Felton, James A. Ferguson, Horatio N. Fraser, C. Dunning French, C. Stanley French, Harry B. French, Howard B. French, J. Hansell French, Harry Fritsch, James A. Garvey, George T. Gwilliam, George Haffa, A. M. Hance, John F. Hancock, F. H. Harmening, G. B. Heckel, Dr. Alfred Heineberg, Charles E. Hires, David H. Holcombe, Hibbert P. John, Hon. Isaac Johnson, C. Mahlon Kline, Christopher Koch, Henry Kraemer, Milton Kutz, R. H. Lackey, Chas. H. LaWall, William E. Lee, Charles Leedom, Joseph L. Lemberger, Robert C. Lippincott, Edward T. Longstreth, Clement B. Lowe, Clement W. Lowe, William E. Lucas, Paul L. McConomy, William McIntyre, Rushton Marot, Dr. R. V. Mattison, Harry Matusow, Alfred Mellor, C. Carroll Meyer, Dr. Adolph W. Miller, Frank X. Moerk, Frank E. Morgan, H. K. Mulford, E. E. Nice, O. W. Osterlund, Dr. Ross V. Patterson, J. W. Rabe, J. P. Remington, Hon. John E. Reyburn, Howard Rohrer, Dr. George D. Rosengarten, Walter A. Rumsey, Saml. P. Sadtler, Dr. Nathan C. Schaeffer, Ralph C. Sharadin, Clayton F. Shoemaker, Richard M. Shoemaker, Walter V. Smith, Rev. David M. Steele, Henry C. Stewart, Dr. P. Samuel Stout,

F. P. Stroup, Henry P. Thorn, Benjamin M. Thorpe, Wallace S. Truesdell, S. E. Uhler, Joseph L. Wade, Walter F. Ware, William Waterall, Dr. Charles A. Weidemann, C. T. Wetherill, W. H. Wetherill, Dr. William P. Wilson, Dr. Alfred C. Wood.

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A. W. Miller, M.D.
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Wallace Procter, Ph.M.
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C. Stanley French
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Henry Kraemer, Ph.D.
Richard M. Shoemaker, Ph.G.
Walter V. Smith, Ph.G.
Otto W. Osterlund, P.D.
Miers Busch, Ph.B., Chairman.

In connection with this entire movement, to do honor to the President of the Philadelphia College of Pharmacy, many letters were received, which we regret we cannot take the space at this time to publish; but all of these have been placed together and deposited with the other historical material of the College.

The portrait has been placed in a prominent position in the Library of the College, and reflects credit upon the members of the College and Alumni who have so unselfishly and zealously contributed to this testimonial. Henry Kraemer, Secretary.

PHARMACEUTICAL MEETINGS.

January meeting.—The fourth of the series of pharmaceutical meetings was held on Tuesday, January 18, 1911, with Prof. C. B. Lowe in the chair.

Dr. Horatio C. Wood, Jr., read a paper on "The Keeping Qualitites of Ergot and its Fluidextract," which is published in the April issue of this Journal (see page 172). The paper was discussed by Mr. W. L. Cliffe, Mr. E. M. Boring, Dr. C. A. Weideman, Mr. John K. Thum, and Prof. Kraemer. Mr. Cliffe called attention to the fact that the fixed oil of ergot is used to some extent in the preparation of certain "Hair Oils." Dr. Weideman referred to the value of ergot as a hæmastatic in hemorrhages of the lungs.

February meeting.—The fifth of the pharmaceutical meetings was held on February 15, 1911, with Mr. Wm. M. McIntyre in the chair.

Mr. Geo. M. Beringer, Jr., presented a paper on "The Extemporaneous Preparation of Medicated Gauzes," which was illustrated with a large number of samples, and also gave a demonstration of the preparation of medicated gauzes. The paper is published in full in the April issue of this Journal (see page 178) and ought to be of very great interest to Pharmacists, as well as physicians and shows what can be done by the retail pharmacist. These formulæ might well be included in the National Formulary, or even be made official, as we find in very many of the foreign pharmacopœias formulæ for the preparation of medicated gauzes. The paper was discussed by Mr. O. W. Osterlund, Mr. E. M. Boring, and the chairman of the meeting.

In the course of the discussion, one of the important points brought out was the superiority of the gauzes made by Mr. Beringer as compared with the general appearance of those found on the market.

NOTES AND NEWS.

Baseball in Colleges of Pharmacy.—When we consider the place that departments of physical instruction hold in our leading educational institutions, it is but natural to suppose that the future historian will consider the peculiar conditions under which this department was introduced into colleges of pharmacy. There have been

a number of brief references in this JOURNAL to the work that the Philadelphia College of Pharmacy has instituted (see this JOURNAL, Vol. 82, p. 545, and Vol. 83, p. 91). While all of the students of the College undergo a physical examination and receive instruction in physical culture, some of them engage in special team work. The baseball team of the P. C. P. played the second of what promises to be, we hope, in the nature of an annual "Harvard-Yale" game with the College of Pharmacy of the City of New York, at South Field, Columbia University, on Friday afternoon, April 14. We publish the following account of the game from the *New York Sun:*

Philadelphia College of Pharmacy baseball team defeated the New York College of Pharmacy team yesterday afternoon for the pharmaceutical championship in a six-inning game, which was played on South Field, Columbia University, in a driving rain, the Philadelphia College of Pharmacy scoring 7 runs, while the New York College of Pharmacy, which is an adjunct of Columbia, could make only 3. The druggists from the Quaker city had the better of it in every department of the game, and although the New Yorkers took the lead in the first inning, they could not hold it long, and Philadelphia won easily.

The home players did their best work in the first inning, when they brought two runs across the plate and shut out the visitors. In the second session they found themselves shut out while Philadelphia made one run, and in the next inning another zero for New York and two tallies for Philadelphia gave the Quaker dispensers the lead. The game was virtually decided in the fourth when a batting rally, two of the hits being three-baggers, added three runs to the Philadelphia score. In their half of the inning the home players made their last run of the game, while the visitors made another in the fifth session. Both teams failed to score in the sixth and as the players were beginning to find it almost impossible to disentangle their feet from the mud, the game was called.

Hart and Gray were the stars of the game, and it was their heavy hitting that won the game for Philadelphia. Each made two three-base hits, and Hart in the fifth hit the ball hard enough for a clean home run, but omitted to touch third in making the circuit and was called out by the umpire. Hancock, who pitched for the winners, had good control of the ball in spite of the wet weather, and allowed only three scattered hits. New York used two pitchers, Steiert and Billings. All of Philadelphia's runs were made while Steiert was in the box.

Yesterday's game was the second annual contest, the game last year, which was played in Philadelphia, also resulting in a victory for the Quakers.

The score by innings:

							R.	H.	E.
Philadelphia	0	1	2	3	1	0	7	7	2
New York	2	0	0	1	0	0	3	3	4

Batteries—Hancock and Hart; Steiert, Billings and Neundorfer.

THE AMERICAN
JOURNAL OF PHARMACY

JUNE, 1911

DRIED MAGNESIUM SULPHATE.

By W. A. Puckner and L. E. Warren.

The Committee of the American Pharmaceutical Association for standards of unofficial drugs and chemical products having considered "Dried magnesium sulphate" the subject was assigned to the senior author of this paper as referee for the preparation of tentative standards. Accordingly provisional academic standards for the substance were prepared and submitted for criticism to a number of manufacturers of chemicals and to several chemists whom it was thought would be interested. At the same time several brands of the product were purchased and examined.

Dried magnesium sulphate is official in several of the foreign pharmacopœias. In the Pharmacopœia formerly official in Austria the method directed for the preparation of the product was to dry the crystallized magnesium sulphate first upon the water bath with stirring and then on a sand bath until a loss of 43 per cent. should be attained. The composition of the residual salt was supposed to correspond approximately to the formula $MgSO_4 + H_2O$. Such a salt should contain about 87.0 per cent. of anhydrous magnesium sulphate. In the last edition of the Austrian Pharmacopœia it is directed to dry the salt on the water bath at 100° with stirring until 36 per cent. of the original weight has been lost. The formula of such a salt should be approximately $MgSO_4+2H_2O$, corresponding to about 77.0 per cent. anhydrous magnesium sulphate. The directions given by the German Pharmacopœia (ed. 5) are to dry the salt in a porcelain dish on a water bath until it has lost from 35 to 37 per cent. of its weight. Such a salt should contain from 75.15 per cent. to 77.54 per cent. of anhydrous magnesium

sulphate ($MgSO_4$) yet the purity rubric demanded by this same authority is only 70 per cent. of anhydrous substance. The salt is also official in the Swiss Pharmacopœia, the method of preparation being similar to that prescribed in the German Pharmacopœia except that the crystallized salt is allowed to effloresce in the air before heating.

Dried magnesium sulphate was prepared by several methods. The first was by the method prescribed in the German Pharmacopœia. This consists in drying the crystallized salt on the water bath with stirring until the substance has lost from 35 to 37 per cent. of the original weight. Owing to the time required it was found impracticable to dry the crystallized salt on the water bath until the specified loss had cccurred. A specimen of 50 gm. of the commercial salt was dried in this manner during several working days and the loss amounted to but 33.7 per cent. instead of a minimum of 35.0 per cent. A duplicate lost 33.8 per cent. in 45 hours drying. Magnesium sulphate was determined in this specimen and 75.2 per cent. of the anhydrous salt found. When dried at 100° in the air oven for 4 hours a loss of 3.4 per cent. was noted in the same specimen.

Dried magnesium sulphate was also prepared by heating 100 gm. of crystallized magnesium sulphate in an air oven, first at a temperature of 60–70° and then at a gradually rising temperature until the specimen practically ceased to lose weight. A loss of 41.2 per cent. was noted. Several days' heating at a temperature of 100° with occasional maxima of 110° failed to secure a loss of 43 per cent. as required by the former Austrian Pharmacopœia (corresponding to the formula $MgSO_4.H_2O$). This specimen contained 84.7 per cent. anhydrous magnesium sulphate.

The most satisfactory method of preparation was found to be to dry the crystallized salt at a temperature of 60–70° with stirring and finally at 100° until a loss of 37 to 40 per cent. had been obtained. A specimen so prepared which had been dried until 39.9 per cent. of the original weight had been lost contained 81.9 per cent. of anhydrous magnesium sulphate.

Three specimens of dried magnesium sulphate bearing the labels of as many makers were purchased on the open market and examined with reference to their content of anhydrous magnesium sulphate and to their loss when dried at 100°. Apparently as a protection against moisture all of the specimens purchased had

been wrapped in paper before being packed in the containers. Two of the latter were composed of thick pasteboard and the other of tin with a close fitting cover.

The magnesium, both in the laboratory specimens as prepared and in the specimens as purchased, was weighed as magnesium pyro-phosphate, the method being described in detail in another part of this paper. It was found that constant weight could not be attained when drying the commercial salt at 100° (at least during no reasonable length of time), the specimens continuing to lose weight very slowly even when dried for several days. It was therefore found expedient to record the results after drying for 4 hours at 100°.

The specimen bearing the label of the Mallinckrodt Chemical Works contained 67.2 per cent. anhydrous magnesium sulphate and lost 7.3 per cent. of water. The Powers-Weightman-Rosengarten specimen contained 64.9 per cent. anhydrous magnesium sulphate and lost 19.4 per cent. on drying. The Merck specimen contained 54.3 per cent. anhydrous magnesium sulphate and lost 26.1 per cent. on drying. While no claim for purity or strength is made upon the label of this specimen, the product sold by this firm is described in Merck's Index (1907) as containing about 2 molecules of water, corresponding to about 77.0 per cent. of anhydrous magnesium sulphate. The product as actually sold, therefore, contains but about 70.5 per cent. of the amount of anhydrous magnesium sulphate claimed for it. The results obtained for all of the specimens examined are tabulated below:

Laboratory number or brand.	Anhydrous magnesium sulphate ($MgSO_4$)	Water (Loss in 4 hours at 100°)
1 (Ph. G. V.)	75.26	3.4
2	84.68	Not determined
3	8.2	Not determined
M. C. W.	67.20	7.29
P. W. R.	64.93	19.42
Merck	54.27	26.16

Tests for heavy metals and for arsenic were made upon all of the specimens examined by methods described in another portion of this paper. The result in each case was negative.

The assertion is made in the literature that dried magnesium

sulphate absorbs moisture when exposed to the air and thus tends to revert toward the crystalline condition. As the crystalline salt is markedly efflorescent when exposed to the air (even losing as much as 7 to 8 per cent. of its weight) it seemed worth while to determine how far the dried salt would absorb moisture. Accordingly a specimen which had lost 41.2 per cent. of the original weight during the process of manufacture, was exposed in a flat-bottomed dish in a place protected from dust and a flat-bottomed dish containing water placed beside it. The water was replenished from time to time as it evaporated and the increase in weight of the exposed salt noted. In two months the specimen weighing 5.0027 gm. had gained 1.813 gm. equivalent to 36.24 per cent. of the original weight.

The examination shows that the dried magnesium sulphate on the American market is far from uniform in composition. This condition might be explained from the lack of authoritative standards for the product in this country. Since magnesium sulphate is usually administered in solution and since the dried salt contains only about 50 per cent. more of real magnesium sulphate ($MgSO_4$) than the official crystallized one it would appear that the dried salt is superfluous. Probably for these reasons the manufacturers have not considered the substance of sufficient importance to subject its manufacture to proper laboratory control.

Based upon the provisional academic standards as first prepared but modified as found necessary by the results of the experimental work, and by the suggestions offered by those to whom the provisional description was submitted for criticism,* the following standards for dried magnesium sulphate are suggested:

Dried Magnesium Sulphate—Magnesii Sulphas Exiccatus. Magnesium Sulphate dried at 100°C. corresponding to from 77.5 to 81.5 per cent. absolute magnesium sulphate.

Dried magnesium sulphate may be prepared by heating (with stirring) 100 parts of crystallized magnesium sulphate in a tarred porcelain dish in a drying oven first at a temperature of 60° to 70° and then at a gradually rising temperature until the substance has lost from 37 to 40 per cent. of its weight.

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* Our thanks are due to those manufacturers and chemists who have made suggestions and criticisms in the preparation of the provisional standards for dried magnesium sulphate.

A fine white powder, without odor, and having a cooling, saline, bitter taste. It is almost completely soluble in water. When exposed to air it absorbs moisture.

An aqueous solution of the salt (1 in 40) should be neutral to litmus paper.

When mixed with ammonium chloride test solution and ammonia water, the aqueous solution of the salt (1 in 40) yields with sodium phosphate test solution, a white, crystalline precipitate. With barium chloride test solution the aqueous solution of the salt yields a white precipitate insoluble in hydrochloric acid.

Ten c.c. of the aqueous solution of the salt (1 in 200) should not respond to the time limit test for heavy metals prescribed in the United States Pharmacopœia, 8th Revision. Five c.c. of the aqueous solution of the salt (1 in 40) should not respond to the modified Gutzeit's test for arsenic, United States Pharmacopœia, 8th Revision.

If from 0.200 gm. to 0.300 gm. of dried magnesium sulphate be dissolved in 50 c.c. of water, the solution filtered if necessary, and if 10 c.c. of ammonium chloride test solution, 10 c.c. of sodium phosphate test solution and sufficient ammonia water to render the mixture alkaline, be added in the order named, shaking after the addition of each reagent, the mixture allowed to stand for 12 hours, the precipitate collected in a tarred Gooch crucible, washed with 1 per cent. ammonia water until free from chlorides, dried, heated to low redness for 15 minutes, cooled and weighed, the weight of the resultant magnesium pyrophosphate should correspond to at least 77.5 per cent. of pure anhydrous magnesium sulphate ($MgSO_4$).

FROM THE LABORATORY OF THE
AMERICAN MEDICAL ASSOCIATION.

THE PERMANGANATE TEST FOR COCAINE.

By FRANCIS J. SEITER.

The behavior of cocaine with potassium permanganate was first described by F. Giesel.[1] He found that the crystalline precipitate of cocaine permanganate is very stable compared with the corre-

[1] Giesel—*Pharm. Zeit.* 1886 p. 132; also, *Chem. Centralbl.* 1887, p. 1448.

sponding salts of the majority of alkaloids and suggested it as a means of identifying cocaine.

Allen states [2] that Beckurts and List, working with cold saturated aqueous solutions of the hydrochlorides of the alkaloids to which was added decinormal solution of permanganate, drop by drop, observed immediate reduction, with separation of brown manganese oxide, in the cases of quinine, cinchonidine, cinchonine, cinchonamine, brucine, veratrine, colchicine, coniine, nicotine, aconitine, physostigmine, codeine and thebaine. Gradual reduction was caused by atropine, hyoscyamine, pilocarpine, berberine, piperine and strychnine. Morphine yielded a white precipitate of oxydimorphine while apomorphine immediately reduced the reagent with green color formation. Narceine, papaverine and narcotine yielded precipitates which decomposed upon addition of more than a few drops of permanganate.

Recently, Saporetti found [3] that B-eucaine would not decolorize permanganate solution while the other cocaine substitutes, A-eucaine, nirvanine, stovaine and alipine gradually decolorized the reagent.

In a previous paper in this Journal, it was reported that five drops of 1 per cent. potassium permanganate were immediately reduced by 1/2 c.c. of a 2 per cent. solution of holocaine, acoine and euphthalmine while gradual reduction occurred in the cases of stovaine, A-eucaine and B-eucaine.

The permanganate test, as described by Giesel, was as follows: one centigram of the hydrochloride of cocaine was dissolved in one or two drops of water and 1 c.c. of 3 per cent. potassium permanganate solution was added. The precipitate of cocaine permanganate formed instantly. Lyons recommended [4] the use of strong cocaine solution and decinormal permanganate. It was found that 2 per cent. solutions of cocaine yielded a precipitate after a short time, but with 1 per cent. solutions, the crystals only formed when the solution was allowed to evaporate.

Inasmuch as the success of the test requires a considerable amount of cocaine, it is not surprising that Sonnié-Moret [5] found the reaction of no value in toxicological examinations. The test has, therefore, been abandoned, where small quantities of the alka-

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[2] Allen, Comm. Org. Anal. 2nd Ed. Vol. III pt. II, p. 144.

[3] Saporetti. *Boll. Chim. Farm.*, 48, 479; also *Chem. Abstr.* 5, 762.

[4] A. B. Lyons—Am. Jour. Pharm. 1886, 240.

[5] Sonnié-Moret, *Chem. Centralbl.*, 1893. 1 p. 859.

loid are concerned, in favor of the gold chloride and platinum chloride tests.[6]

Recently, the writer has studied the action of permanganate solutions of various concentrations upon solutions of cocaine for the purpose of increasing, if possible, the delicacy of the test.

When neutral solutions of cocaine were used, it was found that the limit of precipitation was reached when the solution contained 1 per cent. of cocaine hydrochloride and this was true whether five drops of a 1 per cent. or 1 c.c. of saturated, permanganate solution was added.

Acid solutions of cocaine hydrochloride were next treated with the permanganate solutions. It was found that acidity of the liquid favored the precipitation of cocaine permanganate. After several trials with various concentrations of acid and permanganate, acidity corresponding to 1 per cent. sulphuric acid, and a volume of saturated potassium permanganate equal to that of the cocaine solution yielded the best results.

The test as now used in this laboratory is then as follows: To 1 c.c. cocaine solution, add one drop of 25 per cent. sulphuric acid and 1 c.c. saturated potassium permanganate solution. After standing some time, a drop of the liquid is removed to a slide, cover glass adjusted, excess of liquid removed and a drop of water drawn under the cover glass by means of a piece of filter paper placed on the opposite side. The slide is then examined under the microscope for the characteristic violet-red rectangular plates of cocaine permanganate.

Working in the manner above described, the writer has detected cocaine in 1 c.c. of solution which contained .00033 gram cocaine hydrochloride, equivalent to 1 in 3,000.

The other common natural alkaloids and cocaine substitutes above mentioned, with the exception of A- and B-eucaine, when treated as in the above test were instantly oxidized. The two eucaines reduced the permanganate very slowly.

A-eucaine yielded very small irregular masses of violet-red leafy crystals in 1 per cent. solutions. In high dilutions (1:600) the crystals were better formed and resembled those of ammonium magnesium phosphate. The limit for the formation of the A-eucaine permanganate crystals is 1:5000.

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[6] See Am. Jour. Pharm., Vol. 83, p. 195.

B-eucaine yielded minute violet-red globules, which did not crystallize on standing, in 1 per cent. solutions but not with lesser concentrations.

The crystals were examined under a magnification of 80 diameters in all cases, except the A-eucaine crystals, which required use of a higher power.

CHEMICAL LABORATORY,
DEPARTMENT OF HEALTH, CHICAGO.

MAGMA MAGNESIA.*

By S. L. HILTON.

(REVISED FORMULA)

Magnesium Sulphate, U.S.P.	350.	Gm.
Sodium Hydroxide,	119.	"
Gelatin,	.150	
Distilled Water, q. s.		
	1000.	Cc.

Dissolve the Magnesium Sulphate in 400 Cc. of distilled water, filter the solution through paper, dissolve the gelatine in 50 Cc. of hot water and add this solution to the Magnesium Sulphate and then wash the filter with several portions of distilled water using in all not more than 250 Cc.

Dissolve the Sodium Hydroxide in 400 Cc. of distilled water and when the solution has cooled add 300 Cc. of distilled water, mix thoroughly and when both solutions have cooled to the room temperature, add the solution of Sodium Hydroxide to the solution of Magnesium Sulphate by some means that will deliver the solution of Sodium Hydroxide in rapid drops. Stir the Magnesium Sulphate solution briskly until all of the Soda solution is added, then dilute with distilled water to make the mixture measure 3000 Cc.

Let stand until the precipitate has settled to the 1000 Cc. mark on the container, siphon off the supernatant liquid and add 2500 Cc. of water, stir well and set aside to settle again to the 1000 Cc.

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* Presented at the April, 1911 meeting of the City of Washington Branch of the American Pharmaceutical Association.

mark, again siphon off the supernatant liquid and add 2500 Cc. of distilled water, stir well and set aside to settle to the 1000 Cc. mark, siphon off the supernatant liquid and dilute the magma with distilled water until it measures 4000 Cc., stir well and set aside to settle to the 1000 Cc. mark, draw off the clear liquid, mix the magma well and assay by the process given, and dilute if necessary so that the preparation will contain 7.5 per cent. $Mg\ (OH)_2$.

ASSAY PROCESS.

To 10 Cc. accurately measured in a cylinder and washed, with several portions of distilled water, into a titrating flask add two drops of Phenolphthalein T. S. and 30 Cc. of Normal Sulphuric Acid V.S. the solution is then heated to insure complete reaction, and titrated back with Normal Potassium Hydroxide V.S. to the neutral point, the amount of Normal Potassium Hydroxide V.S. used deducted from the amount of acid previously added gives the amount Normal Sulphuric Acid required to neutralize the Magnesium Hydroxide present, which should be at least 26. Cc. Normal Sulphuric Acid V.S. corresponding to 7.5322 per cent. of Magnesium Hydroxide held in suspension.

With this formula and the process of assay it will be an easy matter to always make a product of definite strength and one that is always uniform.

A DELICATE TEST FOR ACETANILID.

By G. N. Watson,
Assistant in Drug Laboratory, University of Kansas.

Acetanilid when heated together with Boric Acid over naked flame until the Boric Acid melts produces a yellow residue having a peculiar fragrant odor suggestive of Sweet Clover or Arbutus. The yellow color, however, is produced by either Acetanilid or Phenacetine. Antipyrine produces a pink color and a Naphthalene-like odor. Phenacetine produces an odor but characteristic of itself, more faint than that produced by Acetanilid or Antipyrine. With mixtures of the Three Antipyretics, the fragrant odor produced by the action of the Acetanilid is sufficient to produce the characteristic

odor, which is intensified by adding a few drops of water to the residue.

This test suggests the use of Acetanilid as a test for Boric Acid, the delicacy of which is worthy of investigation.

March 22d, 1911.

PHARMACEUTICAL LEGISLATION AS APPLIED TO REGISTRATION AND ADULTERATION.

By Allen C. Thomas, Esq.

I deem it both an honor and pleasure to speak to this body of under-graduates. Our relationship will continue to be most pleasant as long as it is confined to occasions of a social, educational and scientific character. Far better that the pharmacist and lawyer meet as Knights of the Round Table than in the lists. Better to discuss the purposes and effects of legislation in the academic forum than to test their authority in the legal forum. Upon the theory of that old pharmaceutical adage, " An ounce of prevention is worth a pound of cure."

When your course shall have finished and your term of practical experience completed you will first apply for a certificate authorizing you to engage in business and thereafter your fitness will be determined primarily by your possession of such a certificate. The law requires that every proprietor, manager and qualified assistant having a certificate of registration shall display it in some conspicuous place in the retail drug store or pharmacy which he or she shall own or be employed.

In the State of Pennsylvania the authority to grant and issue such certificate is vested in the State Pharmaceutical Examining Board. The title is somewhat suggestive of the origin and purpose of the Board, *i.e.,* that of examining applicants for registration. To this feature of their duty I shall first direct your attention. Since the creation of the Board its functions have been extended and in addition to regulating the status of the pharmacist personally, the regulation of his business has also been placed under the control of this Board and of this regulation I shall speak secondly, indeed the subject will naturally present itself to you in this order as you will first consider qualifying to hang out your

shingle as pharmacist and secondly, conducting and operating your business in accordance with the law.

A word, therefore, concerning the Board to which you must shortly be introduced. It consists of five members appointed by the Governor from the most skilful retail apothecaries actually engaged in business in the State of Pennsylvania having at least ten years' experience. The Board is required to keep a book of registration in which is reported the name and address of each and every person duly qualified to conduct and carry on the retail drug and apothecary business or to hold the position of qualified assistant therein. Meetings of the Board are held every three months at such places as they deem expedient to conduct examinations on the basis of which certificates are granted as the case may be, either to registered managers or qualified assistants: such certificate is then good and sufficient evidence of registration. The following requirements are made of those applying for examination as qualified assistants, first, that they produce evidence of not less than two years' experience and pay the sum of $3.00 for examination and $5.00 for certificate and registration. For those applying for examination of registered managers satisfactory evidence of not less than 4 years' practical experience and paying a fee of $3.00 for examination and $12.00 for registration and certificate.

Now as to the relative effect of these two classes of certificates. No drug store or pharmacy can be conducted without a Registered Manager. The law, *i.e.*, the Act of Assembly does not prescribe the respective rights and duties of these classes in so many words, but that it makes the distinction is clearly seen and therefore practically leaves the determination of the matter to the constituted authority which it has empowered to enforce the Act, *i.e.*, the State Pharmaceutical Examining Board. Consequently the Board has held that the qualified assistant is to act only in the temporary absence of the Registered Manager. The failure of the law to define their respective rights and duties as well as the difficulty of determining the extent of authority exercised in any particular case by the qualified assistant has hindered the Board in the strict enforcement of their views in this matter.

The usual case of violation found is that of a Registered Manager who has two or more stores where he attempts to conduct them with only the assistance of qualified assistants, presuming that his qualification will extend authority to stores which he supervises

but in which he is not actually engaged. Presuming this condition is reported to the State Board, they will at once send their Agent to make a purchase of some drug or to have a prescription compounded and to secure a conviction. The purchase must be made at a time when the Registered Manager is elsewhere. Should he happen to be in this store at the time or should the Agent not be able to prove his absence the prosecution would fail as it must be established beyond a reasonable doubt that there was no Registered Manager present at the time of such sale.

The requirement that every drug store shall be in charge of a Registered Manager has been very effectivly enforced by the Board throughout the State so that at present there are few instances of violation in the larger cities. In other parts of the State, however, where the field is less attractive to the competent and qualified clerk or where detection and prosecution is difficult because of lack of information or inaccessibility, there are still frequently reported cases of attempted evasion of the law which makes necessary occasional crusades of prosecution in order to awaken the dormant conscience to a sense of duty and responsibility.

Just at this point a word that may be seasonable. Many an appeal for a competent clerk comes to the members of the Board and by reason of its familiarity with conditions generally the Board is in a sense an employment agency operated for the good of the individuals concerned and the State as well.

Another phase in the matter which may occur to you, *i.e.*, the case of a person who has no certificate or technical knowledge of the business owning a store. There is nothing to prevent this and in fact it has been decided where the question was raised in the case of Commonwealth vs. Zacharias reported in Volume 181 of the Pennsylvania State Reports, page 126, in 1897, "that the Act of Assembly seeks to regulate only the management of a retail drug store and does not prohibit a passive ownership, so in this case although the defendant was not a pharmacist and operated a chain of stores, the fact that each store was in charge of a Registered Manager prevented conviction and no prosecution could be sustained against him from the mere fact of ownership.

The restriction of the business to such as are qualified is doubly effective, protecting both the public and the profession. In the latter case excluding those who have not earned protection through study and experience. The Act reads " No person shall hereafter engage as

Manager in the business of an apothecary or pharmacist or of retailing drugs, chemicals, and poisons or to compound and dispense the prescriptions of physicians either directly or indirectly without having obtained such certificate." Just here you should note how complete is the language of the Act in the use of the words "compounding and dispensing." The Pennsylvania Board takes the view that compounding is limited to mean the assembling or mixing of the component ingredients, while dispensing includes all that is necessary to the act of filling the order and placing it in the hands of the purchaser.

There are certain exceptions mentioned in this Act where drugs may be dispensed by others than those holding certificates. First, physicians so far as they supply their own patients; second, makers and sellers of patent medicines, and third, storekeepers dealing in and selling the commonly used medicines and poisons.

This latter exemption has been the subject of much criticism and it seems to me justly. The prime object of the law being to safeguard the community—it seems eminently proper that the sale of poisons at any rate should be confined to the competent and qualified pharmacist so that every sale of a poison would be subject to the same degree of care and regulation as that exercised by the pharmacist.

The Act of 1887 after defining poison as "any drug, chemical or preparation which, according to standard works on medicine or materia medica, is liable to be destructive to adult human life in quantities of 60 grains or less," required affixing to the container a label containing the word "poison," the name of the article, and the name of the seller, place of business and further that the seller must satisfy himself that such poison is to be used for legitimate purposes. In addition the pharmacist must keep a poison register in which is to be entered in the case of sales of poison known to be destructive to human life in quantities of five grains or less, the name of the seller, the name and residence of the buyer, the name of the article, quantity sold or disposed of and the purpose for which it is said to be intended.

As to the first exemption in favor of physicians. I believe the sentiment among physicians is against dispensing their own medicines and where the allopath does supply his patients with medicine, it is largely because his homœopathic brother has forced the competition, yet the physician is only paying back in kind for has not

the pharmacist often suggested the remedy and himself prescribed the cure. I cannot see any particular public good to be obtained by the elimination of this clause.

Respecting the other exemption in favor of preparatory remedies or so-called patent medicines. While no reason exists for confining their sale to registered pharmacists there was ample need for regulation of another kind and it has at last been effected through the regulation respecting adulteration.

Now to treat of this important phase of legislation affecting the druggist or pharmacist, *i.e.*, adulteration. Along this line within recent years there has been great development and it has followed generally the trend of an enactment striking at unscrupulous commercialism and constantly unmasking the wolves in sheep's clothing. An era of more honest dealing in drugs as well as other commodities has been inaugurated and the punishment of adulteraters and misbranders is having a wholesome effect whereby a manufacturer, seller and consumer have all been benefited.

The first important act regulating the business of the dealer in drugs was that of May 24, 1887. Section 9 of this Act provided that " No person shall knowingly, wilfully or fraudulently falsify or adulterate or cause to be falsified or adulterated any drug or medicinal substance or any preparation authorized or recognized by the Pharmacopœia of the United States or used or intended to be used in medicinal practice nor mix or cause to be mixed with any such drug or medicinal substance any foreign or inert substance whatsoever for the purpose of destroying or weakening its medicinal power and effect and wilfully, *knowingly or fraudulently sell or cause the same to be sold for medicinal purposes.*" And this was the whole law on the subject of adulteration at that date and as such was inadequate in view of the fact that a person so adulterating must be proved to have done so with a wilful and deliberate intent so that the enactment was intended to strike at the abuse through correction administered to the pharmacist for his wrongful action, but this was insufficient to protect the public for which reason the later act of May 25, 1897, was passed in which the question of intent was eliminated and thereby the regulation made solely to protect the public and a fixed standard is established whereby the term drug is made to include any medicinal substance or preparation authorized or known to the Pharmacopœia of the United States, or the National Formulary or the American Homœopathic Pharma-

copœia or the American Homœopathic Dispensatory and the following five clauses enacted covering the possible ways in which the adulteration might occur, *i.e.:*

1. If any substance or substances have been mixed with it so as to depreciate and weaken its strength, purity or quality.

2. If any quality, substance or ingredient be abstracted so as to deteriorate or affect injuriously the quality or potency of the said drug.

3. If any inferior or cheaper substance or substances have been substituted in whole or part for it.

4. If it is an imitation or is sold under the name of another drug.

5. If the drug shall be so altered that the nature, quality, substance, commercial value or medicinal value of it will not correspond to the recognized formulæ or tests of the latest edition of the "National Formulary," or of the "Pharmacopœia of the United States," or the "American Homœopathic Pharmacopœia," or the "American Homœopathic Dispensatory," regarding quality or purity.

Prosecutions under this Act raised several important questions. In the first place you will note that the drug must correspond in all respects to the recognized formula or tests of the latest edition of the several authorities mentioned. Counsel seeking to make defense for their client charged with violation of this Act asserted that the Act was unconstitutional for several reasons, first, because it incorporated into the law a series of books hence the public were not informed of the text of the law except by going outside of the statute books whereas Article 3, Section 6 of the Constitution provides "No law shall be revived, amended or the provisions thereof extended or conferred by reference to its title only and so much thereof as is revived, amended, extended or conferred shall be re-enacted and published at length." In considering their objection the court held that the Act referred to certain well-known medical books as standards for the definition of the word drug and also for the definition of that which shall be deemed an adulteration of a drug, that this was not in any sense an attempt on the part of the Legislature to revive or amend a law or to extend or confer the provisions thereof by reference to title only. That where impracticable either to publish at length the Court would not consider reference of this character unconstitutional.

Again, it was argued that the act delegated the power of making

the law to a body other than the Legislature; that the makers of the pharmacopœia were virtually invested with legislative functions in contravention of the Constitution, Article 2, Section 1, which provides that "the legislative power of this Commonwealth shall be vested in a General Assembly, etc. It is a settled axiom that the power conferred on the Legislature to make laws cannot be delegated by that department to any other body or authority." "Where the sovereign power of a State has located the authority there it must remain. The power to whose judgment, wisdom and patriotism this high prerogative has been entrusted cannot relieve itself of the responsibility by choosing other agencies upon which the power shall be devolved nor can it substitute the judgment, wisdom and patriotism of any other body for those to which alone the people have seen fit to confide this sovereign trust." The Court, however, dismissed this contention, holding that the argument was defective considering that the Legislature adopted a standard already established, that there was no delegation of authority; that Act not meaning future standards, but that recognized as the standard at the time the law was made. The latest edition, therefore, meant not those to be in the future, but the edition then in force and effect.

This Act remained the law until the Legislature passed the Act of May 8, 1909 in force and effect on and after October 1, of that year. In the meantime the National Pure Food and Drug Act of 1906 had been passed. Much had been written and said about the injustice of such acts as that of 1897 where the standard was fixed by the several books specified in the Act from which no variation could or would be permitted. The objection was not made without reason and undoubtedly the Legislature was influenced by the number of important considerations to adopt what has been termed a variation provision so that deviation from the standard is now allowed provided the fact be plainly stated. It was urged that an iron-clad standard was un-American in that, first, it would stifle research, restrict progress and destroy incentive to advancement: second, however far-sighted, learned and skilful were the makers of the standard, they had neither the whole knowledge nor the last word—third, that the trade would be left with valuable dead stock and in conclusion, that the object of the law was to give what you have so frequently heard called "a square deal." Hence it is that in the Pennsylvania Act no official drug shall be deemed to be

adulterated if the standard of strength, quality or purity be plainly stated upon the bottle, box or other container. Freedom of manufacture and sale is thereby obtained together with the protection of the public by truthful statements accompanying the article.

Certain exceptions in which there may be no variation, however, are specified, *i.e.*, official preparations of opium, iodine, peppermint, camphor, ginger and ethol nitrite. In these instances the law is iron-clad and no deviation permitted. In another respect this Act settled a disputed point raised under the Act of 1897. Under the former Act certain manufacturers and dealers in this State were making and selling inferior preparations of standard articles but labelling them in a manner so different as to claim they were not U. S. P. For Tincture of Ginger, which is usually labelled "Essence of Jamaica Ginger," they made a preparation consisting principally of capsicum, grains of paradise or other pungent or hot drug and water with just sufficient alcohol to keep it from souring and a small quantity of ginger to impart certain of the characteristics of the genuine article was labelled "Climax Picnic Ginger," "Gilt Edge Ginger," etc. So also an article labelled "Camphorated Oil" was said not to be the same as "Linimentum Camphoræ," consequently the standard might be different from that required for the U. S. P. article, so that their article was not to be included in the class condemned, but the Court determined, as the recent Act has declared, thus placing the matter beyond dispute, that an article shall be deemed to be misbranded if it be an imitation of or offered for sale under the name of another article.

The important consideration under the present law is the matter of labelling or branding regarding which the State Board has laid down certain specific requirements. The enforcement of the act is delegated to the State Pharmaceutical Examining Board, which, for this purpose, is authorized to make uniform regulations in order to carry out its provisions and to employ such agents, chemists, attorneys and assistants as may be necessary. Accordingly rules and regulations were at once framed, adopted and published and copies of the same may be secured upon application to any member of the Board.

Hardly had the rules and regulations been promulgated when certain of the latter were attacked and it became a subject for much consideration to what extent the Board were warranted in going, *i.e.*, when the article differed in strength, purity or quality

from the pharmacopœial standard, did the language of the Act requiring the fact of difference to be plainly stated, justify the Board in requiring the use of the words "Not of official strength" and indeed in any instance if the vendor had printed on the label what was to his mind a plain statement although not in the form directed by the Board, might it not still be sufficient in the eyes of the law; at least these are the questions very shortly to arise in prosecutions recently instituted by the State Board.

At once certain manufacturers claimed that a hardship was imposed upon them when they were compelled to print a different label for every State in which their sales were made. In Pennsylvania, where the regulation required the words in certain instances, "Not Official Standard" necessitated the printing of a separate set of labels, cartons, containers, and literature, etc., for every sale made within the confines of the State of Pennsylvania, different from that used elsewhere. To this reply was made that since no other State could legitimately object to this language, the hardship was not as great as appeared on first impression. And they were advised to adopt the Pennsylvania form generally.

With changes so rapid in so diversified a country, with so many sovereign communities there is bound to be difference of opinion, failure to keep pace with the times; special interests undeservedly protected, all producing a lack of uniformity in legislation and diversity in the execution of the law. Nowhere is this better illustrated than in the case of manufacturers who furnish their products to retailers in 48 different States, subject to a variety of legislation and still greater variety of regulation so that a general law enforced through uniform regulations is a consummation devoutedly to be wished for, although hardly likely to be achieved while the States are independent sovereigns.

Some measure of co-ordination might be accomplished by the general adoption by the States of the national law, then by means of a parliament of Pharmaceutical Boards to harmonize the various views and opinions represented there might be evolved a comprehensive and uniform system for their enforcement throughout the United States.

While this discussion in some respects wants application to you as individuals, yet it may offer new avenues of thought suggestions of matters concerning your brethren which the minute they do apply become intensely real and important.

BOOK REVIEWS.

MUNICIPAL CHEMISTRY. A series of thirty lectures by experts on the application of chemistry to the city, delivered at the College of the City of New York. Edited by Prof. Charles Baskerville, New York and London: McGraw-Hill Book Company. 1911.

This book is the outcome of a course of lectures authorized by the Board of Trustees of the College of the city of New York, which were intended to enlighten the public as to what is being done for the municipality of the city of New York to safeguard health, facilitate traffic and add to the pleasures and comforts of life. While the lectures were open to the students of the college as well as the public, a laboratory course of instruction was provided for the senior student who elected the course, thus making it one of the most fruitful of instructive courses that have heretofore been attempted. At first glance the book would seem to be of more special interest to the chemist, but it will be found of very great value also to pharmacists, physicians, leaders in civic movements and all those who desire correct information on the scientific work which is being done in New York City and its application in raising the efficiency of the people and saving the lives especially of the innocent.

ALLEN'S COMMERCIAL ORGANIC ANALYSIS. Vol. iv. Resins, india-rubber, rubber substitutes and gutta-percha, hydrocarbons of essential oils, ketones of essential oils, volatile or essential oils, special characters of essential oils and tables of essential oils. Fourth edition, entirely rewritten. Edited by W. A. Davis and Samuel S. Sadtler. Philadelphia: P. Blakiston's Son & Co. 1911.

This is another of the volumes of Allen's Commercial Organic Analysis that will be welcomed by pharmacists who desire to be kept informed on the newer analytical methods which may be employed in the testing of the products which they handle. The monograph on the "Resins." is the work of Dr. M. Bennett Blackler and in it will be found very many useful hints regarding the examination of such commercial products as asafetida, turpentine, colophony, mastic, etc. The chapter on "India-rubber, Rubber-substitutes and gutta-percha" has been written by E. W. Lewis and of course will be especially valuable to the analyst who engages in the somewhat difficult work of examining rubber compounds.

Dr. T. Martin Lowry is the author of the chapters dealing with the "hydrocarbons and ketones of essential oils"; Mr. Ernest C. Parry has prepared the general monograph on "volatile or essential oils", while the "special characters of the individual essential oils" has been left in the hands of Dr. Henry Leffmann and Prof. Charles H. La Wall. While probably nothing, that has been done in the study of essential oils, can compare with the publications of Schunniel & Co., yet the subject is one of such great importance that analysts welcome the contributions from all practical writers, particularly when methods and results are presented in a readily available form as we find them in this volume.

A Research on the Pines of Australia. By Richard T. Baker, F.L.S., and Henry G. Smith, F.C.S. Published by authority of "The Government of the State of New South Wales." Sidney: William Applegate Gullick, Government Printer. 1910.

This is another one of those comprehensive and illuminating publications that has emanated from the Technological Museum, New South Wales. Here are two earnest workers, who are distinguished by reason of their earlier work on the "Eucalypts and their essential oils" (see this Journal, Vol. 76) and who have now completed a "self-imposed and arduous task" which was made possible by the help and assistance of the higher officers of the Department of Public Instruction. This recent work of Baker and Smith, like their previous monograph on the Eucalypts will endure and is an example to individuals and governments if they would do something that is worth while. As Linnaeus well said in one of his addresses while professor in the University of Upsala, "to do great things one must leave little things alone."

The authors state that of the 32 genera described in Bentham and Hooker's "Genera Plantarum," 11 are found in Australia and Tasmania. As a result of their studies these genera are presented in the following sequence: *Callitris* with 18 species; *Actinostrobus* with 2 species; *Diselma* (*Fitzroya*) and *Microcachrys*, each with one species; *Athrotaxis* with 3 species; *Araucaria* and *Agathis* with 2 species each; (*Dacrydium*) with 1 species; *Pherosphæra* with 2 species; *Phyllocladus* with 1 species, and *Podocarpus* with 5 species.

It is of interest to note that while the work is entitled "A Research on the Pines of Australia," not a single representative of

the *Abieteae,* which includes the genus *Pinus* with its 70 or 80 species and " having the greatest geographical range of the whole order," is found in the territory covered by the authors.

The order of investigation has been as follows: 1. Historical botany of the species. 2. Systematic descriptions. 3. Leaves and fruits: *a,* economics; *b,* anatomy; *c,* chemistry of the oils. 4. Timber: *a,* economics; *b,* anatomy; *c,* chemistry of its products; *d,* forestry. 5. Bark: *a,* economies; *b,* anatomy; *c,* chemistry of its products. 6. Illustrations, to aid in the study of the letterpress.

In summarizing their results the authors state that " botanically the results of the research were generically greater than those specifically, for the peculiarities of structure were found to be quite characteristic of, and differing from, those of cognate genera. Chemically and economically they promise to be of great importance and to open up new fields of commercial enterprise."

They reiterate their belief in taxonomic work which considers the chemical properties and physical characters of the plant constituents along with botanical characters, and state " species so founded give practically constant results, and preserve specific characters throughout their geographical distribution." On this basis they divide the species of the large genera *Callitris* into three groups and give a table showing the probable evolution of the species.

Several new compounds are reported as present in the Australian Coniferales, but perhaps the most interesting discovery is that of a manganese compound in practically all of these trees, and which the authors believe is an essential constituent of them. This compound gives to the wood a darker color and corresponds to what has been regarded as " resin " by previous workers.

The illustrations are very numerous and very excellent, being half-tone reproductions of the living plants, photo-micrographs and color plates of microscopic sections.

PROGRESS IN PHARMACY

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

By M. I. Wilbert.

The first anniversary of the United States Pharmacopœial Convention appears to have been the occasion for an unusual number of interesting happenings bearing on the Pharmacopœia of the United States, its scope, uses, standing in law and the progress of the present revision of the book.

Not the least important of these several items is the renewed interest that is being manifested in the scope of the Pharmacopœia and the possible uses of the book as a basis for rational instruction in materia medica.

Dr. Arthur Dean Bevan, in his address as Chairman of the Council on Medical Education of the American Medical Association, in referring to this need says:

"A limited list of drug preparations containing only those which are most useful and important, is of particular value to medical education at the present time. With the overcrowded condition of the medical curriculum, it is highly important that the small amount of time which the student has to devote to the study of drug preparations should be largely spent in obtaining a thorough knowledge of the more important drugs rather than in the obtaining of a superficial knowledge of all drugs, the majority of which are of little or no value."

The members of the Association of American Medical Colleges, present at the annual meeting held in Chicago in February, 1911, also discussed the various phases of the same question and unanimously adopted a resolution asserting that the use of a small but representative group of medicaments in teaching pharmacology and materia medica is conducive to scientific progress in therapeutics.

U.S.P. Scope.—An editorial (*J. Am. M. Ass.*, 1911, v. 56, p. 1269) discussing the scope of the next Pharmacopœia, asserts that although the Committee of Revision of the United States Pharmacopœia was appointed nearly a year ago, it has issued no report to show what progress has been made, and points out that the Committee should realize that the medical profession is interested as never before as to what should be added to, or deleted from,

the next edition of the Pharmacopœia. Physicians frequently accept at their face value claims made by interested persons regarding the therapeutic action of certain drugs, and there is a tendency on the part of certain doctors to prescribe such drugs, even after they have been admitted to the official standard and consequently included in text-books.

Another editorial (*J. Am. M. Ass.*, 1911, v. 56, pp. 1198–1199) in discussing the standardization of digitalis, asserts that one of the greatest handicaps to exact drug therapeutics is the fact that "impressions" either of the physician or of the patient play such an important part. Many other branches of medicine have been put on a truly scientific basis as a result of careful quantitative work, in either the laboratory or the clinic, or in both, but in drug therapeutics, such expressions as "the drug seemed to do good," are constantly used without the slightest attempt to measure any tangible effect, or to compare the case under treatment with one running a natural course.

A suggestion of the widespread confidence in so-called "clinical" observations is embodied in the remarks of a reviewer in the *British Medical Journal,* who, in dealing with the fifth edition of Professor Cushny's book, says:

"We cannot close the book without feeling how great would be the advantage to medicine if such an authority as Professor Cushny could be provided with access to the wards of a hospital, so that his profound pharmacological knowledge should receive more of the clinical 'salt,' which could not fail to render it the more serviceable."—*Chem. and Drug.*, 1911, v. 78, March 18, p. 50.

Scope of the German Pharmacopœia.—Ernst Gilg, in commenting on the drugs in the Ph. Germ. V, asserts that the one exception that he has to make is that the revisers of the Pharmacopœia, in selecting articles to be included in the book, have shown a woeful lack of system. He expresses the belief that it is about time that books of the importance of pharmacopœias be divorced from personal likes and dislikes, and that the scope at least be based on broad general principles that should be followed throughout.—*Ber. d. pharm. Gesellsch.*, Berl., 1911, v. 21, p. 11.

Importance of the Pharmacopœia.—Oscar Oldberg, in an address on the importance of the pharmacist to mankind, makes a number of reasonable and sane statements regarding the scope of the Pharmacopœia. He points out that the very life of pharmacy

depends upon the Pharmacopœias, and asserts that the pharmacists of America have contributed much to make the Pharmacopœia of the United States respected. Upon examination it is found that the National Pharmacopœias, whatever else they may contain, include the longest known and most thoroughly tested drugs and medicines which, having won and retained the approval of the medical profession, may be said to represent the "survival of the fittest." In that respect the Pharmacopœias are admirable. Nearly all of the twenty national Pharmacopœias, however, have published and do publish recipes for quack nostrums which men ought to know are used only by the very ignorant. Some of the nostrums put in the Pharmacopœias a century ago when actually employed by those who then practised the art of healing are still retained in these books in this age of highly developed medical knowledge when physicians treat them with the contempt such rubbish merits. —*Bulletin of Pharmacy,* May, 1911, pp. 202–203.

U.S.P. AS A LEGAL STANDARD.—As a part of their defense in a suit under the provisions of the Food and Drugs Act, Lehn & Fink enter a demurrer in which the constitutionality of the Food and Drugs Law is attacked on three separate and distinct grounds, which, briefly, are as follows: (1) Because it delegates legislative power, which under the Constitution of the United States belongs exclusively to Congress, to changing, private bodies, not created by, or subject to, the control of Congress. (2) Because it is an ex post facto law in that it specifies that the Pharmacopœia used must be one "official at the time of investigation," and (3) because the act seeks to deprive a citizen of his property and liberty without due process of law.—*Oil, Paint and Drug Reporter,* March 6, 1911, p. 7.

In overruling the demurrer of the defendant, Judge Hough points out that the food and drugs act merely decrees that medicines must conform to the implied standards under which they were sold; that if they were sold under the titles of the Pharmacopœia and the National Formulary they must conform to the standards embodied therein and that this does not constitute a delegation on the part of Congress of its legislative functions to an irresponsible body. In overruling the second contention Judge Hough held that the phrase "official at the time of investigation" must be held to mean official "at the time the goods are shipped," re-

gardless of when the actual analyses or examination might be made.—*Ibid.*, March 27, 1911, p. 9.

Digest of Comments.—The volume of Digest of Comments on the Pharmacopœia of the United States of America (Eighth decennial revision) and the National Formulary (Third edition) for the calendar year ending December 31, 1908, has just appeared as Hygienic Laboratory Bulletin No. 75. The book comprises a total of 564 pages and, in addition to references to criticisms on the pharmacopœia, also includes practically all the available references on the origin, composition and uses of official articles. As a reference book for the active worker in branches related to pharmacy this volume should prove to be of value, while for those directly interested in the Pharmacopœia and the National Formulary, the book should be an inexhaustible mine of suggestions for practical work and original investigations.

Prof. Oldberg.—The remarks by Prof. Oldberg referred to above were made in connection with the celebration of the twenty-fifth anniversary of the School of Pharmacy of the Northwestern University, at which time Prof. Oldberg celebrated the twenty-fifth anniversary of his connection with the school, and retired from the deanship because of his continued ill health. To American pharmacists who have had the pleasure of meeting Prof. Oldberg, his enforced retirement from active work at this time will appeal as a great loss to American Pharmacy. Prof. Oldberg occupies a peculiar and altogether unique place in American Pharmacy and his ideals will no doubt serve as an inspiration to future generations. To those who have had the pleasure of meeting Prof. Oldberg, his quiet and dignified strength, his clear foresight and his positive ways will long appeal. His many friends who were unable to take part in the well-merited tribute recently paid him in Chicago will join in wishing him many years of continued activity for the uplift of American Pharmacy.

New School of Pharmacy.—A news item in a recent number of the *Druggists Circular* (May, 1911, p. 269) contains the announcement of a proposed department of pharmacy in connection with the Fordham University School of Medicine. The course as outlined will lead to two degrees, that of bachelor of pharmacy and that of doctor of pharmacy. The bachelor's degree will require attendance during three full terms aggregating 1,475 hours of instruction, and the subjects taught will include: general,

analytical, organic, and pharmaceutical chemistry, physics, botany, zoölogy, materia medica, pharmacy, bacteriology, experimental pharmacology, food and drug examination and clinical pathology. The subjects of instruction for the doctor's degree will include all of the above together with physiology, physiological chemistry and hygiene; attendance at anatomy lectures, demonstrations and recitations will also be required.

While, theoretically, this proposed course in pharmacy would be a decided and timely forward step in pharmaceutical education, there can be no question as to the impracticability of attempting to develop a really high-class course in pharmacy unless the university itself is in position to adequately endow the school so as to make it entirely independent of the fees to be secured.

Medical Education.—An editorial commenting on an article in the *Wiener Klinische Wochenschrift,* on American Medical schools points out that the diploma mill and the commercial medical school are unknown in Europe. The ignorant but mercenary physician is justly regarded there as a grave social danger. In these directions we have much to learn from Germany. Only by the establishment and maintenance of high standards of medical education can we hope to retain the respect of other nations and to effect those "speedy and radical reforms" which conditions demand.—*J. Am. M. Ass.,* 1911, v. 56, p. 1043.

Present Day Conditions of Pharmacy.—In an address delivered at the joint meeting of the Wayne County Medical Society and the Detroit Retail Druggists Association, Henry P. Hynson of Baltimore, asserts that the hindering practices that retard the accomplishment of idealistic conditions, in the practice of pharmacy are largely due to incompetency on the part of pharmacists, and the inability on the part of some of the physicians to appreciate creditable pharmaceutical attainments or to differentiate between the true and false in pharmacy.

In commenting on the political drawbacks to progressiveness in Pharmacy, he asserts that the American Pharmaceutical Association has not had the support and interest of pharmacists it deserves. It needs stirring up; its enemies, if it has any, are not sufficiently active to give it healthy exercise. It is cursed with politics, conservative, self-preserving, holding back politics, not that "go ahead," "do something" kind, which has made so much out of the American Medical Association and done so much with it. That kind of

politics, if it is politics, would do the American Pharmaceutical Association good, a good deal of good.—*N. A. R. D. Notes,* May 11, p. 335.

Los Angeles Meeting of the American Medical Association.—The issue of the Journal of the American Medical Association for May 20, 1911, appears as the Los Angeles number, and in addition to a number of illustrations and a description of the City of Los Angeles, also contains the preliminary programme for the section meetings. From the number of papers to be presented it would appear that the Los Angeles meeting of the American Medical Association will be not only an unusually interesting one, but also well attended, and if the preliminary programme is an indication of the possibilities of the meeting itself the latter should be epoch-making.

Reformed Almanac as a Health Evangelist.—An editorial (*J. Am. M. Ass.,* 1911, v. 56, p. 1115) calls attention to the January-February number of the Virginia Health Bulletin which is issued in the form of an almanac and quotes a number of advisory aphorisms such as "A dirty well is more dangerous than a dirty kitchen," "Good water is one of the best insurance policies a family can carry," "Wire screens in the window keep crape from the door," "A light overcoat is better than a heavy cold," "It is better to sleep in the fresh air than the fresh grave," and concludes that the Virginia Department of Health deserves hearty congratulations for its success in reforming one of our oldest family institutions and converting it into an evangel of health.

The "World" Sensation.—The sensational charges of incompetency and criminal carelessness of retail druggists brought by the *New York World* have been liberally discussed in drug journals, both in this country and abroad.

Xrayser II, in commenting on the so-called "exposé" believes that rubidium iodide is just about "the limit" as a test for the accuracy of dispensing. He thinks such a test prescription could not have been better chosen if the *New York World* had intended to defeat the very object which it had in view, and in one sense this is satisfactory, for the campaign to prove that druggists as a class are inaccurate or careless dispensers or willfully fraudulent was unworthy to start with.—*Chem. and Drug.,* 1911, v. 78, April 29, p. 115.

"PATENT" MEDICINES AND PRICE PROTECTION.—An unusual amount of publicity has been given to the Supreme Court decision in connection with the direct contract price protection plan of the Dr. Miles Medicine Company.

The publicity that has been given to the decision in the lay journals cannot be said to be creditable to or of advantage to the best interests of the drug trade generally. The *Druggists Circular* (May, 1911, p. 238), in commenting on the evident tendency of the proprietary medicine branch of the retail drug business says:

"The retail drug trade has many heavy loads to carry at best; it should not unnecessarily handicap itself by appearing as a supporter and defender of the makers of nostrums whose sale is regarded as 'contrary to public policy.'"

PROPRIETARY MEDICINES IN THE UNITED STATES.—W. A. Puckner, in an article published in "*Progress,*" (London, England, April, 1911), discusses the proprietary medicine situation in the United States, and points out that in many respects we in this country are far ahead of England and some of the continental countries in combating the proprietary medicine evil. This is particularly true of proprietary medicines supplied through physicians. Even the leading medical journals in Great Britain and on the continent of Europe generally, accept advertisements of the patent medicine type of proprietaries, while in the United States many if not all of the medical journals have eliminated from their advertising pages at least the worst of this type of preparations.

COCA COLA CASE.—An unusual amount of space has been devoted in American drug journals to the discussion of the now famous coca cola case. The *Druggists Circular* (May, 1911, v. 55, p. 274) reports that Judge Sanborn, who was conducting the trial, decided that the Government had failed to establish an actual violation of the letter of the food and drugs act by the coca cola manufacturers, and dismissed the case. One of the most interesting features of the trial was the large array of expert witnesses on each side. The case fell through, seemingly, because of a confusion in the minds of some of the prosecuting witnesses between what the law actually prohibited and what they thought it ought to prohibit.

N.N.R.—To insure a more wide-spread distribution of N.N.R. the American Medical Association has included a reprint of this publication as a supplement to the *Journal of the American Medical*

Association for April 15, 1911. The supplement includes all of the material published in N.N.R. and a complete index which makes the pamphlet available for reference.

An editorial (*J. Am. M. Ass.*, 1911, v. 56, p. 1112) commenting on the publication, reviews the history of the Council on Pharmacy and Chemistry, and recommends that the supplement be critically examined and especially is it urged that physicians read the rules which are printed in the front of the book, bearing in mind that these rules represent the principles on which a preparation is accepted or rejected.

Ph. Germ. V.—The new German Pharmacopœia has been perhaps more actively discussed in European drug and pharmaceutical journals than any Pharmacopœia published up to the present time. Much of this discussion has been of a critical nature and some of it caustic, but all of it no doubt will prove beneficial either directly or indirectly and should go far toward making the next edition of the German Pharmacopœia even more representative of the best in the practice of medicine and pharmacy.

A recent article in the *Chemist and Druggist* (1911, v. 78, April 29, pp. 139–142) discusses the new galenical preparations that have been included in the Ph. Germ. V, and points out that only a limited number, some 20 in all new galenical preparations are represented in this Pharmacopœia.

Canadian Formulary.—An editorial review of the third edition of the Canadian Formulary of Unofficial Preparations, published by the Authority of the Ontario College of Pharmacy, in the *Chemist and Druggist* (1911, v. 78, April 29, pp. 146–147) calls attention to some of the many changes and reprints a number of new recipes and alterations.

Metric Prescriptions.—The conclusions of the Council of the British Medical Association on the adoption of the metric system of weights and measures by medical practitioners in prescribing and dispensing, are reprinted (*Pharm. J.*, Lond., May 6, 1911, p. 585) as follows:

"The Council recognizes that the full and complete adoption of the metric system in practice depends upon its being made the system according to which students are trained, and therefore recommends that the teaching, both theoretical and practical, in pharmacology and materia medica, should henceforth be according to the metric system." The Council also outlines a transitional

procedure suggested for adoption by medical practitioners and presents the following recommendations:

1. That the teaching both theoretical and practical in pharmacology and materia medica should henceforth be according to the metric system.

2. That medical practitioners should now write their prescriptions in metric form, and that, to facilitate this, mixtures should be ordered in sixteen-dose bulk, and pills or powders should be ordered in tens.

3. That dispensers should be instructed that every prescription written without symbols is to be dispensed in metric measures.

4. That the divisions should take the matter into consideration, and, if they think desirable, confer with the pharmacists in their area.

Pharmaceutical Preparations.—The chemical laboratory of the American Medical Association (*J. Am. M. Ass.,* 1911, v. 56, p. 1344) presents an additional contribution on commercial tablets of bismuth, opium, and phenol, and graphically illustrates the composition of these tablets as claimed by various manufacturers and the composition actually found in the laboratory.

An editorial in the same *Journal* (pp. 1334–1335) points out that for some years past pharmaceutical houses have put out in tablet form an enormous number of combinations of drugs of real or fancied value. In many instances the combinations are not suited to the tablet form and it is not surprising that many of these tablets do not conform to the composition that is claimed for them. It is not to be inferred that the manufacturers willfully put up products that are false to label, but rather that many of the combinations are pharmaceutical impossibilities. That is to say, it is pharmaceutically impossible—or at least commercially impracticable—to manufacture, in tablet form some of the combinations that are listed in the manufacturers' catalogues.

Doses.—An editorial (*J. Am. M. Ass.,* 1911, v. 56, p. 1114) discusses the determination of the proper dose of medicine and quotes from Manquat's "Principles of Therapeutics" his opinion regarding the fallacy of undue dependence on medication. The editorial concludes that the principles as stated are correct. The drug is to be regarded only as a staff to assist lightly over the difficult places, and not as a strong crutch to bear the whole burden. First, throw away the pack and the other impediments; give entire

freedom of action to all natural forces; assist by the staff only as actually needed and the steep will be surmounted.

ADRENALIN.—A news note (*Oil, Paint and Drug Reporter*, May 8, 1911, p. 28H), points out that in the final hearing on the alleged infringement of the Takamine patents on glandular extractive products, Justice Hand of the United States Circuit Court found for the complainant on nine of the sixteen claims in the patent specifications in question, in one cause of action, and on four of the eight claims in the other cause. The news item also points out that not all of the claims of either patient were at issue, and that Justice Hand held that the case had to do only with the patent on the product and not that on the process.

EPINEPHRINE.—An editorial in discussing the need for a generic name for the blood-pressure-raising substance of the suprarenal gland, points out that there are thirty or more different brands of solution of this substance on the market, five being in this country alone. The products are identical so far as their chief constituent is concerned; they differ, however, as to the solvent and preservative used. The processes of manufacture of some of them are patented; all of them are sold under trade names. The editorial concludes that it cannot be too strongly emphasized that "Epinephrine" is a true scientific name for the active principle of the suprarenal gland, and that it should be used on all occasions when the active principle and not some particular firm's make is referred to.—*J. Am. M. Ass.*, 1911, v. 56, p. 901.

ASPIRIN.—The Bayer Co., Ltd., in discussing trade-mark rights, points out that as a rule an important trade-mark is the property of a wealthy firm, but none the less it is something that has to be worked for; behind it there is brain and there is energy, and it has had to be paid for. The law supports its rights, and anyone infringing them does so at his peril.—*Pharm. J.*, Lond., 1911, v. 86, March 11, p. 358.

M. Meldrum, in a communication in which he discusses the abuses that have grown out of trade-mark rights in England, asserts that honesty, commercial honesty at least, has become more or less relative. He contends that the royalty or profit of trade-marked articles is out of all proportion to the price paid and the modicum of brain and energy supplied by the holder of the trade-mark, and thinks it high time to consider the possibility of placing some check on the present methods of granting trade-marks or

trade-names in so far as the practice of pharmacy is affected thereby.—*Ibid.*, March 25, p. 424.

BENETOL.—An unsigned article in the "Propaganda for Reform" discusses the claims that are being made for benetol, and concludes that the claim made in the advertising matter that benetol is a newly discovered compound is absurd. It is not a chemical compound but a simple solution of the well-known substance alphanaphthol in the still better-known substances, glycerin, soap and water.—*J. Am. M. Ass.*, 1911, v. 56, pp. 1128–1129.

CAFFEINE.—The article on Therapeutics in the *Journal of the American Medical Association* for May 6, 1911 (v. 56, pp. 1328–1331) is devoted to a discussion of the therapeutics of caffeine. The history of this chemical is reviewed and the pharmacology and therapeutics discussed at some length. Caffeine-containing drugs such as guarana and kola are also discussed.

CARGENTOS.—Cargentos is claimed to be a preparation of colloidal silver containing 50 per cent. of metallic silver in the form of oxide, together with a sufficient amount of modified casein to maintain the silver oxide in colloidal form when in solution.

Cargentos is prepared by precipitating an alkaline solution of silver caseinate and silver oxide by an acid, dissolving the precipitate in an alkali, dialyzing the resulting solution against running water and evaporating the remaining colloidal solution to dryness in vacuo.—*J. Am. M. Ass.*, 1911, v. 56, p. 1460.

COLCHICINE.—Hermann Fühner (*Archiv für Experimentelle Path. u. Pharm.*) considers it necessary to apply biological as well as chemical tests for toxicological determinations of colchicine, since colchicine resists the putrefactive processes of the dead body for several months and certain animal decomposition products give color reactions similar to those of the alkaloid.

CYCLOFORM.—Cycloform is the isobutyl ester of p-amidobenzoic acid, which forms a white crystalline powder, slightly soluble in water, easily soluble in alcohol, ether and benzene. It is a powerful local anæsthetic, and has but little toxic action. It is recommended in the form of a 5-per-cent. ointment or dressing, and is useful in certain skin diseases.—*Chem. and Drug.*, 1911, v. 78, April 29, p. 151.

DIGITALIS.—An editorial (*J. Am. M. Ass.*, 1911, v. 56, pp. 1198–1199) in discussing the standardization of digitalis, calls attention to Hyg. Lab. Bull. No. 74, in which Hale points out that the

view adopted by most pharmacopœias and by the Brussels Conference that leaves of the second years' growth are more potent than those of the first year appears to be founded on tradition only. The view, or rather impression, that the leaves of wild growing plants are more potent than those of the cultivated plants also does not rest on a scientific basis. The editorial concludes that a perusal of this Bulletin will place the practitioner in a much better position to form a judgment of the character of the digitalis preparation he uses and that the work which it embodies should be of value in improving the pharmacopœial requirements of this important drug.

DIGLYCODISALICYLIC ACID.—It is claimed that diglycodisalicylic acid $O(CH_2.COOC_6H_9.COOH)_2$, possesses the full physiological activity of salicylic acid, and has certain advantages over acetylsalicylic acid for therapeutic use. It forms shining, odorless leaflets, with a faint acid taste; it melts at 168–170° C.—*Pharm. J.*, Lond., 1911, v. 86, April 15, p. 498.

OVOGAL.—Ovogal is a combination of bile acids with egg albumen. It is a greenish yellow powder, insoluble in water, dilute acids, ether, benzol, fats, etc. Alcohol and acetone do not dissolve it, but after long action remove from it small amounts of the bile acids. Alkalies dissolve ovogal, splitting it into albumen and bile acids (Glycocholic acid and taurocholic acid).—*J. Am. M. Ass.*, 1911, v. 56, p. 1460.

OXYGEN.—A report of the Council on Pharmacy and Chemistry outlines a description with tests for compressed oxygen (*J. Am. M. Ass.*, 1911, v. 56, p. 813). An editorial (*ibid.*, p. 820) points out that this report describes an article which so far is one of the few things that have not been appropriated by the proprietary medicine houses. Oxygen is often depended upon to save life that is at its lowest ebb, and the purity of the substance is a most important matter, more important than the purity of many official drugs.

PERISTALTIN.—Peristaltin is a glucoside of the formula $C_{14}H_{18}O_8$, extracted from cascara sagrada. It is a yellow powder, soluble in water and in dilute alcohol. It is said to have a marked purgative action.—*Chem. and Drug.*, 1911, v. 78, April 29, p. 151.

PHENOL.—An interesting controversy has grown out of the Ph. Germ. V requirement that phenol should react neutral with litmus paper. Ernst Schmidt (*Arch. d. Pharm.*, 1911, v. 249, pp. 236–240) discusses some of the attacks that have been made on the pharmacopœial statement, and points out that while ordinary

crystalline carbolic does react distinctly acid with litmus paper, it is readily shown that this reaction is not due to phenol but to a contaminating acid, and that ordinary phenol when neutralized with a few drops of alkali, and absolutely pure phenol will comply fully with the Ph. Germ. V requirements.

PANTOPON.—A report of the Council on Pharmacy and Chemistry (*J. Am. M. Ass.,* 1911, v. 56, pp. 1278–1279) discusses pantopon, and points out that this is a preparation of opium, containing a mixture of hydrochlorides of the various opium alkaloids, as extracted directly from the drug with more or less purification. The Council holds that the name does not effectively suggest that the preparation is a mixture of opium alkaloids and that it does not protect the public against habit-forming and other dangers inherent in such mixtures.

PAPINE, a more or less similar preparation, is also commented upon, and an editorial (p. 1268) concludes that pantopon and papine are a menace to the public, and that in spite of the testimonials for both these products it would not be amiss if physicians would continue to use the drugs, morphine and opium, whose value—and dangers—they know.

PHOSPHORUS.—An editorial discussing the possible elimination of white phosphorus in the production of matches, points out that there are about 3,500 employees in 15 of the 17 match factories in the United States. Of 3,383 whose occupation was specified 65 per cent. are exposed to phosphorus fumes; 95 per cent. of the 1,395 women are so exposed. An intensive study of 3 factories was made, and eighty-two cases of necrosis were discovered.—*J. Am. M. Ass.,* 1911, v. 56, pp. 1038–1039.

SACCHARIN.—A widely published news note reports that the Secretary of Agriculture has issued a decision, based upon a finding of the Referee Board of Consulting Scientific Experts, which forbids the use of saccharin in food on and after July 1 next. The decision is under the Food and Drugs Act and will prohibit the manufacture or sale in the District of Columbia or the Territories of foodstuffs containing saccharin, as well as interstate commerce in such footstuffs.

SANATOGEN.—An answer to an inquiry points out that sanatogen is said to contain 95 per cent. of casein so that 30 gm. (1 ounce) of this preparation would contain approximately 28.5 gm. of protein, which would yield 117 calories. This is the equivalent in round

numbers of one-third of a pint of milk or one and one-half eggs. The same amount of energy would be given by an equal weight of starch or by one and one-fifth as much of flour or other cereals. The writer concludes that sanatogen like most preparations of this class while a food is a ruinously expensive one.—*J. Am. M. Ass.*, 1911, v. 56, p. 1345.

Strophanthus.—J. Haycock outlines an assay method for strophanthus seeds, in which after eliminating the oil by means of ether, he extracts the seed with 70 per cent. alcohol and treats the resulting extract with sulphuric acid by means of heat to change the strophanthin into strophanthidin. The strophanthidin is subsequently washed out, by means of chloroform, dried at a temperature below 65° C. and weighed. The resulting yield divided by 0.365 gives the amount of strophanthin present.—*Pharm. J.*, Lond., 1911, v. 86, April 29, pp. 553–554.

Xerase.—Xerase is a mixture of a specially prepared dry beer yeast 150 parts, grape sugar (dextrose) 20 parts, white bole 125 parts and a mixture of nutritive salts 3 parts. Xerase is a yellowish-gray, powder, having a weak odor of yeast and a salty taste. It is only slightly soluble in water. It resists ordinary atmospheric conditions.—*J. Am. M. Ass.*, 1911, v. 56, p. 1460.

THE CITY OF WASHINGTON BRANCH OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

The stated meeting of the City of Washington Branch of the American Pharmaceutical Association for April was devoted to a general discussion on matters of interest to pharmacists.

Dr. Murray Galt Motter discussed the use and advantage of a restricted materia medica and called attention to the efforts that have been and are being made in this country to bring about reforms in therapeutic practices. He pointed out that the need for limiting instruction in materia medica subjects to a restricted list of substances is being recognized by teachers in medical schools and that the general trend of this tendency is well illustrated by the resolution adopted by teachers in the medical schools in Philadelphia at an informal conference called by Prof. Joseph P. Remington, on February 3, 1908.

This resolution, in part, reads as follows:

"*Resolved,* That it is of the utmost importance for accuracy in prescribing, and in the treatment of disease, that students of medicine be instructed fully as to those portions of the United States Pharmacopœia which are of value to the practitioner."

To illustrate the fact that the need for restricting the materia medica taught in medical schools is being recognized outside of our own country, Dr. Motter exhibited a list of titles adopted by the teachers and examiners of the University of London as a basis for examining candidates for degrees as well as licensure. This list was furnished him by Dr. A. R. Cushny who, in a recent interview, assured Dr. Motter that unless the forthcoming edition of the British Pharmacopœia was more limited in scope, and more representative of the best that is available in materia medica, British teachers of the latter subject would find it necessary to ignore the Pharmacopœia entirely, and limit their teaching to the restricted list of medicaments mutually agreed upon.

Dr. Motter expressed the belief that much the same conditions prevail in our own country, and that unless the scope of our recognized National Standards can be restricted to a reasonable number of articles, the books themselves must be ignored entirely by medical schools. He characterized the present Pharmacopœia of the United States as an illustration of "would-be science," the National Formulary as "a hybrid between science and commercialism," and N. N. R. as "a sop to the commercial Cerberus."

In conclusion he pointed out that in the time allotted to materia medica in the present medical curriculum, it is practically impossible to discuss, intelligently, more than a limited number of the more important medicaments and that the resolutions adopted at the recent conferences in Chicago, attended by representatives of various organizations, indicate a rather wide-spread interest in a more restricted materia medica. As an illustration of the tendency manifested, he read the following preamble and resolution adopted at the annual meeting of the Association of American Medical Colleges, held in Chicago, February 27–28, 1911 (*J. Am. M. Ass.,* Chicago, April 8, 1911, v. 56, p. 1065).

"Whereas, The time devoted to the study of pharmacology, materia medica and therapeutics is necessarily limited, and

"Whereas, The thorough knowledge of a small but representative group of medicaments is conducive to scientific progress in therapeutics; therefore, be it

"*Resolved,* That the Association of American Medical Colleges commends to the attention of medical educators and examiners, the limited materia medica lists published by the joint committee of the Council on Medical Education, and of the National Confederation of State Medical Examining and Licensing Boards, and the Chicago Medical Society.

"*Resolved,* That the association urge upon the colleges and the examining boards the necessity for the recognition of the principle underlying these lists, and for the early adoption by the boards of a materia medica list to which licensure examinations shall largely be confined."

The subject was further discussed by Messrs. Kalusowski, Flemer, Hilton, Hunt, and Wilbert, and the general trend of much of the discussion suggested the desirability of having the Pharmacopœia of the United States restricted to important medicaments so that it might serve as the basis for materia medica instruction in medical schools.

Dr. Reid Hunt expressed the belief that, at present, the physician's part in the revision of the Pharmacopœia is but a minor one, and that much of what the better informed medical men might have to say is discounted by the fictitious value that is accorded to the reputed needs of the less conscientious, or less competent practitioner who is willing to continue the use of substances that appear to have no recognizable medicinal value.

Mr. M. I. Wilbert called attention to some of the recent comments that have appeared on this same subject, and quoted Dr. D. L. Edsall who, in his address as chairman of the Section on Pharmacology and Therapeutics of the American Medical Association, points out that the Pharmacopœia of the United States is now used by but few teachers of materia medica and is little known to medical practitioners.

"Revision may make it better or may make it even worse so far as its usefulness to students and practitioners is concerned, according as it is intended to make it purely a reference book or also a practical working book; in other words, whether it is revised upward or downward.

"Unless marked changes are made in it, however, it will remain as it is now, chiefly a name to the vast majority of the medical profession and will render no appreciable service in improving therapeutic practice."

Mr. Samuel L. Hilton reported a series of experiments to determine the most desirable method of procedure for making Magma of Magnesia N.F. He exhibited a number of samples and presented a formula for a preparation that contains considerably more Magnesium Hydroxide than does the one at present official. (See p. 268.)

The Secretary exhibited a number of preparations, made by Mr. Otto Raubenheimer, illustrating some of the additions and changes embodied in the Ph. Germ. V.

He also exhibited a number of samples of Solution of Peptonate of Iron with Manganese N.F., made by Mr. John K. Thum, according to a formula proposed for the N.F., showing the possible variations resulting from slight modification of the method of procedure. Mr. Thum presents a modification of this formula, but ventures the opinion that the formula and method of making proposed by Dunning, in 1905, give much more satisfactory results.

Mr. S. L. Hilton, as Secretary of the Board of Pharmacy of the District of Columbia, called attention to the objections that have been made to a recent ruling of the board that the local dental supply depots could not legally sell narcotic drugs. The subject was discussed at some length, and on motion of Mr. Bradbury, seconded by Mr. Richardson, it was agreed that "the members of the City of Washington Branch of the American Pharmaceutical Association endorse the present efforts of the Board of Pharmacy to enforce the pharmacy laws of the District of Columbia."

M. I. Wilbert, *Secretary.*

PHILADELPHIA COLLEGE OF PHARMACY

The ninetieth annual commencement of the Philadelphia College of Pharmacy was held in the American Academy of Music on Thursday evening, May 25. After a prayer by the Rev. Edwin S. Carson, the degrees were conferred by the President, Howard B. French.

The following are the names of those who received the degree of Doctor in Pharmacy (P.D.), with the subjects of their theses:

Name.	*Thesis.*	*Residence.*
Allison, James Harrison,	Ferri Sulphas Exsiccatus,	Pennsylvania
Atkins, John Walt,	Cacao,	Pennsylvania
Baradofsky, Samuel,	Action of Iodine on Starch,	Pennsylvania
Beckley, Norman Clyde,	Acidum Sulphuricum Dilutum,	Pennsylvania

Name.	*Thesis.*	*Residence.*
Bellitz, Miss Jennie,	Colocynth,	Russia
Berry, DeWilton Snowden,	Drug Store Management,	Maryland
Bloes, Lee Otto,	Vanishing Cold Creams,	Pennsylvania
Bollinger, Chester Eugene,	Physiological Testing of Ointments,	Pennsylvania
Bradley, Kersey Elmer,	Sterilization of Cocaine Solutions,	Pennsylvania
Bradley, Oscar Samuel,	Ergot,	Pennsylvania
Bricker, Robert Osborn,	Cultivation of Atropa Belladonna,	New Jersey
Brush, Franklin Cotton,	Rhus Glabra,	Pennsylvania
Burtt, Lloyd,	Determination of Stearic Acid,	Pennsylvania
Butler, John Albert,	Petrox,	Pennsylvania
Calvin, William Ray (P.C.),	Liquor Potassii Arsenitis,	Pennsylvania
Carey, George Warner,	Hydrastis Canadensis,	Pennsylvania
Carpenter, Pierce Raymond,	Ointment of Mercuric Nitrate,	Pennsylvania
Carrington, Arthur Hudson,	Expressed Almond and Peach Kernel Oil,	New York
Christopher, Louis Edward,	Diluted Hydrochloric Acid,	Massachusetts
Cohen, Philip,	Sapo Mollis,	Pennsylvania
Costenbader, Clayton Elmer,	Hydrastis Canadensis,	Pennsylvania
Crawford, William Burton,	Mel,	Pennsylvania
Davis, Elliot Veil,	Rhamnus Frangula,	Pennsylvania
Donnelly, John Henry,	Liquor Sodae Chlorinatae,	Pennsylvania
Edwards, David Everett,	Rhamnus Purshiana,	Pennsylvania
Eisman, David William,	Olive Oil,	Russia
Ennis, James Henry, Jr.,	Ether,	Pennsylvania
Farrell, Walter John,	Fluidextract of Parsley Root,	New York
Friedman, Nathan Meyer,	Essence of Pepsin N.F.,	Pennsylvania
Gaskell, Walter James,	Elixir Digestivum Compositum,	Pennsylvania
Gault, Claude Ellsworth,	Petrolatum,	Ohio
Gordon, David Harris,	Bay Rum,	Georgia
Greaves, Alvah Frank,	Peanut Oil,	New York,
Greeninger, Charles Wenger (P.C.),	Elixir Ferri, Quininae et Strychninae Phosphatum,	Pennsylvania
Gregory, Harrison W.,	Soft Gelatin Capsules,	Pennsylvania
Haimowitz, Morris,	Calcium Oxalate in Podophyllum,	Pennsylvania
Hancock, Clyde Raymond,	Aletris Farinosa,	Pennsylvania
Hart, Farel,	Solidified Alcohol,	Ohio
Heacock, Clifton Elwood,	Fluidextract of Kola,	Pennsylvania

Name.	*Thesis.*	*Residence.*
Held, John C., Jr.,	Milk—Its Cereal Modification,	Pennsylvania
Hemminger, Robert Elton,	Show Globe Colors,	Pennsylvania
Hendricks, Lyle Vallington,	Aqua Hydrogenii Dioxidi,	Oregon
Herr, Clarence Sloan,	Steel,	Ohio
Hildebrand, Charles Pinkney,	Maize Oil,	North Carolina
Hinski, Herman Leo,	Disastase,	Pennsylvania
Hosfeld, Herman Francis,	Bacillus Acidi Lactici,	Ohio
Johnson, David Emil,	Fluidextracts of Celery and Angelica Root,	Pennsylvania
Kaehler, Carl Frederick,	Sulphuric Acid,	Pennsylvania
Kreamer, Oscar Perry,	Prescription Difficulties,	Pennsylvania
Lathrop, William Norman,	A Saponaceous Dentrifrice Elixir,	Connecticut
Lemen, Hermann Light,	Acidum Hydriodicum Dilutum,	Maryland
Lightner, Walter Irvin,	Chloroform,	Pennsylvania
Longaker, Louis,	Unguentum Resorcini Compositum,	Pennsylvania
Lowe, Edgar Walthour,	Advertising as Applied to Pharmacy,	Pennsylvania
Lynn, Ellsworth Waldemar,	Rhamus Purshiana,	Pennsylvania
McNutt, William Clyde,	Liquor Calcis,	Pennsylvania
Marshall, William Elisha,	Galla,	Pennsylvania
Martin, Joseph Stanislas,	Cultivation of Nicotiana Tabacum in Lancaster, County, Pa.,	Pennsylvania
Martz, Samuel George Washington,	Aloes and Aloin,	Pennsylvania
Melville, Frederick Thornton,	Tobacco and Smokecraft,	Pennsylvania
Messinger, Martin Lester,	Pilocarpus — Its Preparation and Action,	Pennsylvania
Miller, Jacob J., Jr.,	The Physician's Prescription—To Whom Does it Belong?	Pennsylvania
Miller, Noble Collins,	Medicated Waters,	Pennsylvania
Millrood, Samuel,	Fluidextract of Gentian,	Russia
Moore, Albert Worthington,	Alcohol as Sold by Retail Pharmacists,	New Jersey
Morley, John Edward,	Antidiphtheric Serum,	New York
Morris, Edwin Kramer,	Tinctura Iodi,	Virginia
Muthig, Charles,	Sources of Salicylic Acid and Its Uses,	New York
Myers, Louis Henry,	Hydrastis,	Pennsylvania
Neal, Clark (P.C.),	Theobroma Cacao,	Pennsylvania
Oswald, Lewis William,	Glycerin,	New York

Name.	*Thesis.*	*Residence.*
Patterson, George William, Jr.,	Phthalic Acid,	Pennsylvania
Patton, Frank Oakman,	Acidum Nitricum Dilutum,	Massachusetts
Paxson, Leon Kirk,	The Physical and Chemical Constants of Goose Fat,	Pennsylvania
Penney, Theodore Rufus,	Casein Creams,	Oklahoma
Pettit, Albert Worrell,	Tooth Washes,	New Jersey
Phillips, Robert Earl,	Label Paste,	Pennsylvania
Rachmil, Albert,	The Ethics of Harmony Between Two Allied Professions,	Pennsylvania
Ralston, John Morrow,	Syrup of Chocolate as a Vehicle,	Pennsylvania
Rapaport, Julius George,	Strophanthus Kombe,	Russia
Read, Thomas Preston,	Medicine as an Economic Science,	Pennsylvania
Rice, Wallace Stoddard,	Pilocarpus,	Pennsylvania
Riley, Frank Louis,	Fermentation,	Maine
Rogers, Edson William,	Olive Oil,	New Jersey
Rose, William Wilson,	Capsicum in Tincture of Ginger,	Delaware
Rosenberg, Samuel (P.C.),	Camphor Cream,	Pennsylvania
Rothrock, Roswell John,	Fluidextract of Juniper,	Pennsylvania
Rovner ,Israel,	Solution of Calcium Creosote,	New Jersey
Runyan, Edwin Percy,	Theatrical Cold Creams,	Pennsylvania
Ryan, Edward Henry.		Pennsylvania
Sammons, George Israel,	Cannabis Indica,	Pennsylvania
Sands, Paul Douglass,	The Determination of Phosphoric Acid,	Pennsylvania
Sasse, Arno Richard,	Liquid Petrolatums,	Missouri
Schauermann, Howard George,	Glycerinum,	Pennsylvania
Schell, Frank Wacker,	Color Standards for Galenicals,	Pennsylvania
Schmidt, Miss Selma L. (P.C.),	The Testing of Balsam of Peru,	Ohio
Segal, Nathaniel Jules,	Opium,	Pennsylvania
Shaker, Elias,	The Production of Lactic Acid by Tablets Under Differing Conditions,	New York
Shearer, George Keyworth,	Goldner's Test for Cocaine,	Pennsylvania
Shiles, Stanley Andrew,	Acacia and Its Uses,	Delaware
Shugars, George Forrester,	Trillium and Its Fluidextracts,	Pennsylvania
Smith, Edgar Chellis,	Label Paste,	Pennsylvania
Smith, Robert Edgar, Jr.,	Cactus Grandiflorus,	Florida
Snyder, Marshall Prescott,	Essence of Pepsin,	Pennsylvania
Somers, Wilbert,	Cologne Water,	New Jersey

Name.	*Thesis.*	*Residence.*
Southard, Paul Harriman,	The Glycerophosphates,	Ohio
Steelman, Ethelbert,	Syrup of Hydrochlorphosphates,	Indiana
Stein, Morris,	Cold Creams,	Pennsylvania
Strauss, Raymond Albert,	Animal Diastase,	Pennsylvania
Sylvester, William Grimes,	Phenolphthalein—Its Action in the Body,	Pennsylvania
Tanner, Thomas Bernard,	Ergota,	Pennsylvania
Temperton, Leith Sylvester,	Solution of Iron Peptonate and Manganese,	Pennsylvania
Udell, William Howard,	Cocaine and Its Legislation,	Pennsylvania
VanInwegen, Frank P. (P.C.),	Hamamelis Folia,	New York
Verstine, Samuel Philip,	Crystallization,	Pennsylvania
Watkins, Llewellyn James,	The Dispensing Physician,	Pennsylvania
Wear, John,	Liquor Ferri Albuminati,	Pennsylvania
Wepfer, Adolph Gustav,	Baptisia Tinctoria,	Wisconsin
Winter, John Coleman,	Panax Quinquefolium,	Pennsylvania
Wolford, James Scott,	The Abuse of Narcotics,	Pennsylvania
Young, Frank Aloysius,	Cod Liver Oil,	Pennsylvania

The following are the names of those who received the degree of Pharmaceutical Chemist (P.C.), together with the subjects of their theses:

Name.	*Thesis.*	*Residence.*
Charleston, Julius Lewis,	A Tasteless Castor Oil,	Pennsylvania
Duvoisin, Frank,	Carbon Tetrachloride,	Pennsylvania
Flickinger, William Gordon,	Fabrica Farinae,	Pennsylvania
Graeff, William Lewis,	Desiccated Thyroid Glands,	Pennsylvania
Greaves, Mrs. F. Hunter,	Diluted Hydrobromic Acid,	North Dakota
Hartenstein, Earl Stewart,	Liquor Ferri Chloridi,	Illinois
Hedges, Francis Xavier,	Tragacanth and Indian Gum,	Pennsylvania
Kramer, Raymond John,	Tinctura Ferri Chloridi,	W. Virginia
Langton, Daniel Joseph,	Pepsin,	Pennsylvania
Shoemaker, Clayton French, Jr.,	Chemistry of the Vanilla Beans and Manufacture of the Extract,	Pennsylvania

The following were awarded certificates of proficiency in chemistry: Allen, James Henry (P.D.); Denzler, Edward O.; Duvoisin, Charles; Haines, Frank Earl; and Swain, J. Harry.

The certificate in the Pure Food and Drug Course was awarded to Peter Amsterdam, P.P. There were 137 candidates for the degrees *in course,* coming from the various States and countries as follows: Connecticut, 2; Delaware, 2; Florida, 1; Georgia, 2; Indiana, 1; Illinois, 1; Maine, 1; Maryland, 2; Massachusetts, 2; Missouri, 1; New Jersey, 7; New York, 8; North Carolina, 1; North Dakota, 1; Ohio, 6; Oklahoma, 1; Oregon, 1; Pennsylvania, 90; Russia, 4; Virginia, 1; West Virginia, 1, and Wisconsin, 1.

The address to the graduating class was made by Hon. Willis L. Moore who delivered an interesting discourse upon "the weather," discussing some of the more interesting phenomena relating to the physics of the atmosphere and distinguishing between hurricanes, cyclones, tornados and thunder storms.

AWARD OF PRIZES.

The following students received the grade of distinguished: Pierce R. Carpenter and Herman L. Hinski. The grade of meritorious was attained by John A. Butler and Morris Haimowitz.

THE WILLIAM B. WEBB MEMORIAL PRIZE, a gold medal and certificate offered for the highest general average in the branches of committee, operative pharmacy and specimens, was awarded to Pierce R. Carpenter, the presentation being made by Mr. Walter A. Rumsey. The following graduates received honorable mention in connection therewith: Franklin Brush, John A. Butler, Charles P. Hildebrand, Herman L. Hinski, William E. Marshall, Edwin K. Morris, William W. Rose, Paul D. Sands, William G. Sylvester, Thomas B. Tanner, and Adolph G. Wepfer.

THE CHEMISTRY PRIZE, $25, offered by Prof. Samuel P. Sadtler, for knowledge of chemical quantitative analysis, was awarded to Edwin K. Morris. The following graduates received honorable mention in connection therewith: Herman L. Hinski and George K. Shearer.

THE MATERIA MEDICA PRIZE, $25, offered by Prof. Clement B. Lowe, for the best examination in materia medica and in the recognition of materia medica specimens with a meritorious thesis, was awarded to Edwin K. Morris. The following graduates received honorable mention in connection therewith: James H. Allison, John A. Butler, Pierce R. Carpenter, Morris Haimowitz,

Charles P. Hildebrand, Herman L. Hinski, Samuel G. W. Martz, Charles Muthig, Leon K. Paxson, and Adolph G. Wepfer.

The Microscopical Research Prize, a Zentmayer Microscope, offered by Prof. Henry Kraemer for the most meritorious thesis involving original microscopic work, was awarded to Julius G. Rapaport. The following graduates received honorable mention in connection therewith: Jennie Bellitz, Kersey E. Bradley, Morris Haimowitz, Clyde R. Hancock, Herman F. Hosfeld, and Adolph G. Wepfer.

The Analytical Chemistry Prize, $25, offered by Prof. Frank X. Moerk, for the best work in qualitative and quantitative analysis, was awarded to Herman L. Hinski. The following graduates received honorable mention in connection therewith: John A. Butler, Pierce R. Carpenter, Walter J. Farrell, Charles P. Hildebrand, and William E. Marshall.

The Operative Pharmacy Prize, $20 in gold, offered by Prof. Joseph P. Remington, for the best examination in operative pharmacy, was awarded to Thomas B. Tanner, the presentation being made by Dr. E. Fullerton Cook. The following graduates received honorable mention in connection therewith: John W. Atkins, Norman C. Beckley, Franklin C. Brush, David E. Johnson, Oscar P. Kreamer, and Marshall P. Snyder.

The Maisch Pharmacognosy Prize, $20 in gold, established by the late Jacob H. Redsecker, of Lebanon, Pa., and continued as a memorial by his nephew, Jacob Redsecker Beetem, for histological knowledge of drugs, was awarded to William W. Rose, the presentation being made by Mr. Clayton F. Shoemaker. The following graduates received honorable mention in connection therewith: Philip Cohen, Morris Haimowitz, Herman L. Hinski, Edwin K. Morris, and Adolph G. Wepfer.

The Maisch Botany Prize, $20, offered by Mr. Joseph Jacobs, of Atlanta, Ga., for the study of native medicinal plants, was awarded to Adolph G. Wepfer, the presentation being made by Dr. Adolph W. Miller. The following graduates deserve honorable mention in connection therewith: Jennie Bellitz, Morris Haimowitz, Clyde R. Hancock.

The Theoretical Pharmacy Prize, a Troemmer Agate Prescription Balance, established by the late Mahlon N. Kline for the best examination in theory and practice of pharmacy, was awarded to Pierce R. Carpenter, the presentation being made by Mr. C.

Mahlon Kline. The following graduates received honorable mention in connection therewith: Samuel Baradofsky, John A. Butler.

The Commercial Training Prize, $20 in gold, offered by Prof. Joseph P. Remington to the graduate who passed the best examination in commercial training at the final examination for the degree, was awarded to Edwin P. Runyan, the presentation being made by Mr. Warren Poley. The following graduates received honorable mention in connection therewith: John A. Butler, Pierce R. Carpenter, James H. Ennis, Jr., Morris Haimowitz, Herman L. Hinski, Edgar W. Lowe, Frank O. Patton, Roswell J. Rothrock, Clayton F. Shoemaker, Jr., and Robert E. Smith.

The Instructor's Prize, $20, offered by the Instructors of the College for the highest term average in the branches of pharmacy, chemistry, and materia medica, was awarded to Samuel G. W. Martz, the presentation being made by Prof. Freeman P. Stroup. The following graduates received honorable mention in connection therewith: Samuel Baradofsky, Herman L. Hinski, and Edwin K. Morris.

The Pharmacy Quiz Prize, one year's membership in the American Pharmaceutical Association, offered by Prof. Charles H. LaWall for the best term work in theory and practice of pharmacy, was awarded to Samuel G. W. Martz. The following graduates received honorable mention in connection therewith: Samuel Baradofsky, Arthur H. Carrington, Edwin K. Morris, Charles Muthig, and Edwin P. Runyan.

The Kappa Psi Fraternity Prize, a gold medal, offered by the Eta Chapter of the Kappa Psi Fraternity to the graduate making the highest general average during his or her senior year at the College, was awarded to Pierce R. Carpenter, the presentation being made by Dr. George L. Holstein. The following graduates received honorable mention in connection therewith: John A. Butler, Morris Haimowitz, and Herman L. Hinski.

The Athletic Prize, a silver loving cup, offered by Henry S. Godshall, P.D., and John J. Bridgeman, P.D., to the member of the graduating class who, at commencement, stands with the greatest number of points in athletics to his credit and has obtained the highest general average amongst those participating in athletics at the College, is awarded to Clyde R. Hancock, the presentation being made by Dr. William Schleif. The following graduates deserved honorable mention in connection therewith: Kersey E. Bradley,

Robert O. Bricker, Louis E. Christopher, A. F. Greaves, Farel Hart, Herman F. Hosfeld, A. W. Moore, John E. Morley, Louis W. Oswald, Frank O. Patton George K. Shearer, John Wear, and Frank A. Young.

In addition to those above mentioned, a special prize was offered this year. The will of the late George Washington Hayes of Lebanon, stipulated that the gold watch, which he had received as a member of the class of 1882, from Messrs. Allaire, Woodward & Co., for his work on powdered drugs, was to be awarded to the most distinguished student of the class of 1911. This prize was awarded to Pierce R. Carpenter, the presentation being made by Mr. Joseph L. Lemberger.

EIGHTH INTERNATIONAL CONGRESS OF APPLIED CHEMISTRY

At the instance of the representatives of more than 4,000 American chemists, the Congress of the United States by Joint Resolution on March 4, 1909, authorized the President of the United States to invite the Eighth International Congress to meet in the United States. This invitation was extended to the Seventh International Congress in London, June 2, 1909, by the Honorable Whitelaw Reid, Ambassador from the United States to Great Britain, and enthusiastically and unanimously accepted.

The thirteen Delegates sent by the Government of the United States to the Seventh Congress were appointed by that Congress as the nucleus of the Organizing Committee for the Eighth Congress, with power to add to their number.

On June 11, 1910, the gentlemen forming this nucleus met and organized for the despatch of business, and at a meeting held August 26, 1910, greatly increased the membership of the Organizing Committee. These Official Representatives are primarily charged with the responsibility of seeing to it that none of the interests in their respective jurisdictions are overlooked at the Eighth Congress, and that all are properly represented thereat; they also serve as an official avenue of communication between their respective Governments and the Eighth Congress. This enlarged Organizing Committee, on October 8, 1910, provided for

a Constitution and By-Laws, and further provided for 25 scientific Sections and Subsections. One of these—on the leather industries—still remains to be organized if those interested in leather and allied manufactures desire to have a special Subsection in the Eighth Congress. Sectional Executive Committees for each of the 24 Sections and Subsections have been organized. The task of completing the working committees (comprising a total of about 25 members each) for all of these 24 Sections and Subsections is going rapidly forward.

The responsibility for the conduct of the Eighth Congress is vested in the Executive Committee.

The responsibility for the conduct of business before the various Sections and Subsections at their sessions during the Congress is vested in a Committee on Sectional Procedure, which Committee is composed of all the Presidents of Sections and Subsections, and tentative rules have been framed.

The Committees of Sections and Subsections, and particularly their respective Executive Committees, are charged with the responsibility of procuring papers for all their sessions, not only from chemists and others resident in the United States, but also from those resident in all other countries of the world. To the end that the most effective co-operation may be secured, it is earnestly urged that, in all countries outside the United States, there be very soon formed Committees of Sections and Subsections corresponding to those established in the United States, or so many of them as will provide fully for the interests of chemists and allied professional and business men in such countries as ma- not be interested in all the Sections and Subsections of the Eighth Congress, and that, upon organization and announcement of such Committees, all chemists and all chemical and allied societies resident in such country and interested in the Eighth Congress communicate with those of their Committees in whose activities and purposes they are interested, giving the titles and scope of papers or other communications they may contemplate contributing to the Eighth Congress. It is suggested that all such societies within or outside the United States, which desire to co-operate with any particular Section or Subsection of the Congress, communicate that fact to the President of the corresponding American Sectional Committees. It is further suggested that Chairmen of Committees of all Sections and Subsections outside the United States com-

municate, at stated intervals, preferably the first of every month, to the President of the American Committees of the corresponding Sections or Subsections, the titles of papers or other communications promised, together with the names and post office addresses of their authors, so that the American Committee may be able to form an approximate estimate of the probable activities of the respective Sections for the guidance of those responsible for the conduct of the Eighth Congress.

In order that there may be beneficial co-operation and a close affiliation between the Eighth Congress and its Sections and Subsections on the one hand and other scientific or professional bodies meeting in or near New York or Washington at or about the time of the convening of the Eighth Congress, on the other, a Committee on Co-operation has been established; this Committee will be glad to communicate with any such associations in an endeavor to bring about such co-operation.

The President of the United States has shown his deep interest in the objects and purposes of the Eighth Congress by consenting not only to act as its Patron, but also to preside at the Opening Meeting of the Eighth Congress, which is to be held in Washington, D. C., on Wednesday, September 4, 1912. The President of the United States has also shown his great solicitude for the success of the Eighth Congress by causing invitations to be sent to all the Governments of the World to take part in the deliberations and the work of the Congress. The chemists, individually, and collectively as Societies, not only of the United States, but of all other countries of the world, therefore owe it not only to their science and to their profession to exert every effort to make the Eighth International Congress of Applied Chemistry completely successful, but they also owe it to their own countries and their own Governments to use every means in their power to see to it that every interest in their respective countries is properly and fully represented at the Eighth Congress and to demonstrate to their own Governments and their fellow-countrymen that, in accepting this invitation of the President of the United States, the confidence reposed in the chemists of the respective countries by their Governments has been fully justified. To this end the hearty and enthusiastic co-operation of chemists and allied professional and business men, and particularly of societies of chemists, and of allied professional and business societies the world over, and along the

lines suggested at various places in this pamphlet, is most earnestly solicited.

It is hoped that all the matters relating to this Congress will be given the widest possible publicity in all chemical and allied societies, and in all chemical and allied publications the world over, and that suggestions for changes which may more surely assist in the realization of a successful and profitable meeting may be made to the Executive Committee of the Eighth Congress.

Respectfully,

EIGHTH INTERNATIONAL CONGRESS OF APPLIED CHEMISTRY.

EDWARD W. MORLEY, *Honorary President.* WILLIAM H. NICHOLS, *President.*

BERNHARD C. HESSE, *Secretary.*

NEW YORK, March 6th, 1911.

TENTATIVE RULES GOVERNING THE RECEIPT OF PAPERS FOR PRESENTATION OR PUBLICATION

1. All papers should be in the hands of the American Committee on or before July 1, 1912.

2. All such papers should be presented in duplicate, legibly written, but preferably typewritten.

3. Each paper must be accompanied by an abstract thereof, also in duplicate, legibly written, but preferably typewritten.

4. All papers received prior to July 1, 1912, and accepted for publication will be printed prior to the meeting of the Congress and grouped according to the Sections to which they are assigned; papers received after July 1, 1912, and accepted for publication will be printed prior to the meeting of the Congress if practicable, but it cannot be guaranteed that they will be placed in the Section to which they belong, but they may appear in an appendix.

5. The American Committee will neither revise nor edit any papers or abstracts; papers received for publication will be printed *in extenso* as offered, or only the abstract accompanying the full paper will be printed, or the paper will be printed by title only, together with the name and post office address of its author, or the paper will not be printed at all, as may be decided in each case by the Committee on Papers and Publications.

6. Authors will not receive printer's proofs of papers or abstracts submitted; authors must do their proofreading on the manuscript; whatever is printed by the American Committee will be printed in exact accordance with whichever of the authors' manuscripts is selected for publication.

7. Discussions will be recorded in the official language in which they are uttered, and participants in the discussions will have an opportunity of editing the manuscript report of such discussion; the American Committees will print from such edited manuscript report of the discussion, and printer's proofs will not be sent to participants.

8. No paper which has previously been published shall be read at the Eighth Congress nor printed in its final Report without the consent of the Sectional Executive Committee, the Committee on Papers and Publications and the Executive Committees of the Eighth Congress having first been obtained.

NOTE: The American Committee will proceed to print the papers during the first half of July of 1912. The size of the edition printed will be determined by the number of membership fees received on or before July 1, 1912; persons contemplating membership in the Congress should have their membership completed prior to July 1, 1912, in order that they may be sure of receiving a copy of the Report of the Congress; membership fees can be received after July 1, 1912, only as subject to the condition that copies of the Report of the Congress cannot be guaranteed, and will be supplied only until the number of extra copies printed shall have been exhausted.

MERCK'S MANUAL OF THE MATERIA MEDICA. (Fourth Edition.) A Ready Reference Pocket Book for the Physician and Surgeon. Containing a comprehensive list of Chemicals and Drugs—not confined to "Merck's"—with their synonyms, solubilities, physiological effects, therapeutic uses, doses, incompatibles, antidotes, etc.; a table of Therapeutic Indications, with interspersed paragraphs on Bedside Diagnosis, and a collection of Prescription Formulas, beginning under the indication "Abortion" and ending with "Yellow Fever"; a Classification of Medicaments; and Miscellany, comprising Poisoning and Its Treatment; and an extensive Dose Table; a chapter on Urinalysis, and various tables, etc. (Merck & Co., 45 Park Place, New York, 1911. 493 pages. While compiled for the use of physicians, there is much in the book regarding the materia medica, doses, urinalysis, etc., to make it a serviceable reference work for pharmacists also. Sent on receipt of forwarding charges of 10 cents, in stamps, to pharmacists, or to students enrolled in any College of Pharmacy, in the United States.)

THE AMERICAN
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JULY, 1911

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VOLUMETRIC DETERMINATION OF MERCURY.

By Carl E. Smith.
Laboratory of the Powers-Weightman-Rosengarten Co., Philadelphia.

Abstracts of a Report by a Committee of the Division of Pharmaceutical Chemistry of the American Chemical Society have appeared in recent journals (see this Journal, 1911, v. 83, p. 186), the work reported on being a comparison of various methods for the determination of mercury in the medicinal compounds of this metal.

The purpose of these notes is to relate some recent experiences with two of these methods, which are probably the simplest and most reliable of those mentioned in the report, the Hempel method for mercurous and the Rupp method for mercuric compounds. It is desired also to call attention to one other, which is perhaps the best volumetric method available for some purposes.

The writer's experience with the Hempel method, in its application to calomel and mercurous iodide, corroborates to a considerable extent the results of the committee. The objectionable feature of it, noted by several of the members, that long-continued shaking is needed to bring the salt into solution, may be eliminated, it was found, by the simple change of adding the iodine solution first, instead of the potassium iodide. When this is done and the mixture at once shaken vigorously in a stoppered flask, solution is effected very quickly. The final result is the same in either case, as comparative trials have shown. It seems advisable, also, to increase the quantity of sample, to lessen the experimental error, in the case of calomel to about 1 Gm. The most satisfactory results were obtained when working in the following manner: To about 1 Gm. of calomel, accurately weighed, contained in a glass-stoppered 300 c.c.

Erlenmeyer flask, add 50 c.c. of N/10 iodine solution. Mix by rotating until the salt is thoroughly moistened, then add a solution of 2 Gm. of potassium iodide in 10 c.c. of water and at once shake the stoppered flask vigorously until solution is complete. Titrate the excess of iodine with N/10 sodium thiosulphate, using starch solution as indicator, adding the latter when the liquid is nearly decolorized. Each c.c. of N/10 iodine solution consumed corresponds to 0.02355 Gm. of mercurous chloride.

A sample of calomel, practically chemically pure, assayed by this method 99.5 to 100.0 per cent., the average of 6 determinations being 99.7 per cent., with some variation in the working details. Practically the same figures were obtained with yellow mercurous iodide containing slight traces of impurities.

The criticism of the Rupp method, that reduction of the mercury is not complete within a reasonable time without the use of heat and that, when heat is employed, the mercury is not easily dissolved afterwards, is well founded, if Rupp's directions in outlining the method (*Berichte d. d. ch. Ges.*, 1906, v. 39, p. 3702), be taken literally as regards the quantity of alkali to be used. While his directions lead to the inference that only enough is required to combine with the acids formed by the reaction, his figures in the same paper show that he used a decided excess, not less than 10 c.c. of normal solution for 0.2 Gm. of mercuric chloride. The divergent opinions regarding this method by the members of the committee are doubtless due chiefly to differences in the quantities of alkali used. When the above mentioned proportions are taken, the reaction is almost instantaneous, unless the solution is excessively diluted, and may safely be regarded as complete within 5 minutes, without heating. It will do no harm to use a still larger excess of alkali or to let the mixture stand longer. Shaken in a stoppered flask with the iodine solution, the precipitate is then dissolved very readily. A large excess of acetic acid is to be avoided, as it tends to make the result too low, which is also the experience of Mr. L. D. Havenhill, of the committee. The best results were obtained by carrying out the details as follows: Dissolve about 0.5 Gm. of powdered mercuric chloride, accurately weighed, contained in a glass-stoppered 300 c.c. Erlenmeyer flask, in a solution of 2 Gm. of potassium iodide in 10 c.c. of water. Add 25 c.c. of normal caustic alkali solution and 6 c.c. of 40 per cent. formaldehyde solution. Mix by swirling the flask occasionally during 10 minutes, then acidu-

late with about 5 c.c. of 36 per cent. acetic acid. Add 50 c.c. of N/10 iodine solution and shake vigorously in the stoppered flask until the mercury is dissolved. Titrate the excess of iodine with N/10 sodium thiosulphate solution, adding starch solution when the liquid is nearly decolorized. Each c.c. of N/10 iodine solution corresponds to 0.01355 Gm. of mercuric chloride.

Chemically pure mercuric chloride gave by this method 99.8 to 100.3 per cent., with an average of 100.1 per cent. in 5 determinations. Similar results were obtained with mercuric iodide, oxide, ammoniated mercury, and mixtures of mercuric chloride and ammonium chloride colored with aniline dyes. It is the official method of the German Pharmacopœia, 5th revision, 1910, for the assay of mercuric chloride tablets and ointment of ammoniated mercury.

The third method alluded to above consists in the titration of mercuric compounds, in nitric acid solution, with sulphocyanate in exactly the same way as the titration of silver. It is not applicable in presence of chlorides and probably not in presence of other halogens. It was first made serviceable for accurate work by R. Cohn (*Ber. d. d. chem. Ges.*, 1901, v. 34, p. 3502) and simplified by Rupp and Kraus (*Ibid.*, 1902, v. 35, p. 2015). For illustrations of its application see below. The writer has no personal experience with this method, but his associates have found it accurate and useful for the assay of technical mercuric oxide containing iron. The German Pharmacopœia uses it for the assay of several galenical preparations. For the convenience of any readers of this JOURNAL interested in this subject, who may not have access to this book, the assay methods for mercury preparations prescribed therein are given here:

Mercuric Chloride Tablets.—Composed of equal parts of mercuric chloride and sodium chloride, colored with aniline dye. Dissolve 2 tablets of about 1 Gm. each, accurately weighed, in water and dilute to 100 c.c. In 20 c.c. of the solution dissolve 1 Gm. of potassium iodide, add 10 c.c. of a 15 per cent. solution of potassium hydrate and 3 c.c. of a 40 per cent. solution of formaldehyde with 10 c.c. of water. After one minute add 25 c.c. of 30 per cent. acetic acid, 25 c.c. of N/10 iodine solution, and shake until the mercury is dissolved. Titrate the excess of iodine with N/10 sodium thiosulphate solution, using starch solution as indicator. Each c.c. of N/10 iodine solution consumed corresponds to 0.01355 Gm. of mercuric chloride.

Ointment of Ammoniated Mercury.—Consists of 10 per cent. of ammoniated mercury and white vaseline. Heat about 5 Gm. of the ointment, accurately weighed, in a small flask with 25 c.c. of 12.5 per cent. hydrochloric acid on a water bath. Mix frequently by rotating the flask during 10 minutes. Pour the acid liquid into a 100 c.c. flask, rinse the vaseline and flask repeatedly with water and dilute the combined liquid and washings to 100 c.c. Transfer 25 c.c. to a glass-stoppered flask, add 1 Gm. of potassium iodide and proceed further as directed for the assay of mercuric chloride tablets. Each c.c. of N/10 iodine solution consumed corresponds to 0.01257 Gm., approximately, of ammoniated mercury.

Mercuric Salicylate.—Contains about 55 per cent. of mercury. Dissolve about 0.3 Gm. of the salt, accurately weighed, in dilute sodium hydrate solution, acidulate with acetic acid, and add 25 c.c. of N/10 iodine solution. Let the mixture stand in a closed flask for 3 hours at room temperature, rotating it occasionally. Titrate the excess of iodine with N/10 sodium thiosulphate solution. Each c.c. of N/10 iodine solution consumed corresponds to 0.0100 Gm. of mercury.

Mercury Plaster.—Contains 20 per cent. of mercury; made with lead plaster, wool fat and yellow wax. Heat about 3 Gm. of the plaster mass, accurately weighed, with 20 c.c. of nitric acid, sp. gr. 1.38 to 1.40, in a flask having a wide neck and connected with a reflux condenser. Heat about 10 minutes or until mercury globules are no longer visible in the sandy deposit of lead nitrate, add 25 c.c. of water and heat again until the fat has separated, leaving the aqueous layer clear. Cool and pour the solution through a tuft of absorbent cotton into a 100 c.c. flask. Break up the disk of fat, rinse it and the flask with 4 or 5 portions of 5 c.c. each of water and to the combined liquids add potassium permanganate until permanently red or until brown flakes separate. Decolorize or clarify the solution by addition of ferrous sulphate solution and dilute to 100 c.c. To 25 c.c. of the solution add 2 c.c. of a 10 per cent. solution of ferric alum and titrate with N/10 ammonium sulphocyanate. Each c.c. consumed corresponds to 0.01000 Gm. of mercury.

Mercury Ointment.—Contains 30 per cent. of mercury; made with wool fat, peanut oil, lard, and mutton tallow. Proceed as directed for the assay of mercury plaster, using about 2 Gm. of the ointment and 20 c.c. of nitric acid.

Ointment of Red Mercuric Oxide.—Contains 10 per cent. of mercuric oxide; made with white vaseline. Proceed as directed for the assay of mercury plaster, using about 5 Gm. of the ointment and 20 c.c. of nitric acid. Continue heating until the red color of the mercuric oxide has disappeared. Each c.c. of N/10 ammonium sulphocyanate solution corresponds to 0.0108 Gm. of mercuric oxide.

The factors given throughout these notes are based on the atomic weights having O = 16 as the standard. If the volumetric solutions used are made by the H = 1 standard, either the factors or the final results should be multiplied by 0.992.

THE PHARMACOGNOSY OF ECHINACEA.[1]

By Henry Kraemer and Maud Sollenberger.

The root of *Echinacea angustifolia* has been used in certain proprietary medicines for a number of years. It was not until about 1886, however, that the identity of the drug was determined. From specimens of the entire plant which were sent John Uri Lloyd from Nebraska, his brother C. G. Lloyd was enabled to identify the drug as being derived from *Echinacea angustifolia,* or the "Nigger Head" of the West.[2] Apparently considerable quantities of the drug are used, and there are a number of reports to the effect that it is more or less adulterated. It should be stated that while the drug is largely used, the Council on Pharmacy and Chemistry of the American Medical Association[3] has investigated the subject and come to the conclusion that "Echinacea is deemed unworthy of further consideration until more reliable evidence is presented in its favor." However, the plant and drug have a number of interesting anatomical features, and it was deemed advisable to present the results of this study at this time. Authentic specimens of the crude drug were secured from Professor Lloyd. Living plants of *Echinacca angustifolia* were purchased from Mr. John Hellerman, who has been cultivating the plant in Philadelphia, and these plants

[1] Read at the New Jersey Pharmaceutical Association meeting, June 14, 1911.

[2] *Pharm. Review,* 1904 (vol. 22), p. 11.

[3] *Jour. A. M. A.,* Nov. 27, 1909; Report A. M. A. Council on Pharmacy and Chemistry, 1909, p. 144.

have been growing for some time in the garden of the Philadelphia College of Pharmacy and their identity established.

There are two species of *Echinacea* which are indigenous to the United States. These are known by botanists under the generic name of *Brauneria,* although Hoffmann, in the monograph of the Compositæ in Engler and Prantl's Pflanzenfamilien, still retains them under the genus, *Rudbeckia.* Thus we have the following botanical synonyms of the species that concerns us:

Rudbeckia pallida, Nuttall (1834).
Echinacea angustifolia, DeCandolle (1856).
Brauneria pallida (Nuttall), Britton (1904).

DESCRIPTION OF THE PLANT.

Brauneria pallida is a perrenial herb, somewhat resembling *Brauneria purpurea,* a plant that is quite extensively cultivated in the gardens, and known as the "Cone flower." The vertical rhizome and root of *Brauneria pallida* is, however, very much larger than those of the cone flower. The plant is from 3 decimetres to 1 metre high, the leaves are usually more or less crowded near the base of the stem, and from among them arises a long peduncled head of flowers. The leaves are for the most part rather narrow and lanceolate, pointed at both the apex and base, and with a very long petiole, the latter frequently being as long as the lamina. They are nearly entire, and with three prominent parallel veins. The flower heads are made up of both tubular and ray florets, the entire cluster being about 9 centimetres in diameter. The receptacle is conical and solid, and subtended by three series of imbricated bracts which are lanceolate, spinose, with an acute or acuminate apex, and appressed or slightly spreading. On the receptacle are borne numerous purplish tubular flowers, which are about 1 centimetre long and partly enclosed in a somewhat woody bract with a narrow attenuated apex which projects several millimetres above the flowers. The tubular flowers are perfect, the calyx being short and acute, the corolla tubular and the stigmas ellipsoidal. The achenes are obpyramidal and with a pappus, forming a short dentate crown. The ray flowers are of a purplish or rose color, narrow elliptical or linear, about 7 centimetres long, and with two or three acute teeth at the apex. The ray flowers appear to be neutral, and in addition to the spatulate corolla, possess a short calyx tube with five acute, rather short, serrate teeth.

DESCRIPTION OF RHIZOME AND ROOT.

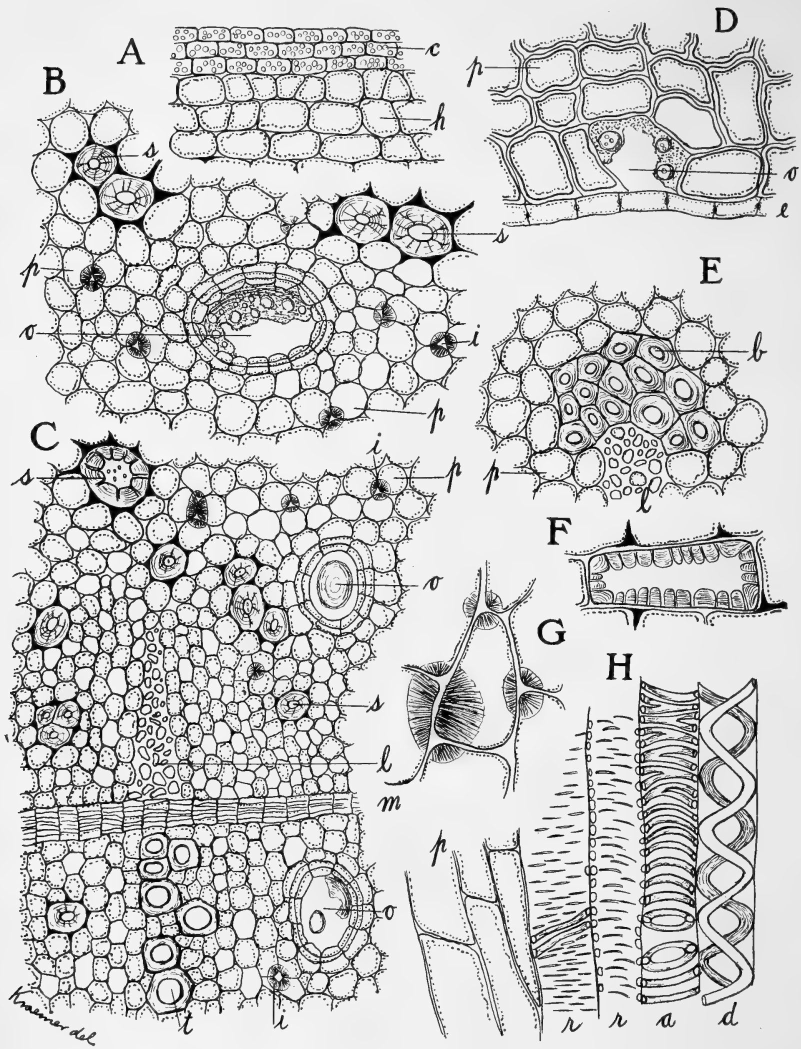
The crown of the rhizome is simple or branched, resembling that of other Compositæ. The underground stem, or rhizome, attains a length of as much as 12 centimetres, and is from 10 to 15 millimetres in diameter. It is slightly annulate, marked by a number of V-shaped stem scars and circular root scars, but otherwise it is nearly smooth and of a somewhat purplish-brown color. The root is continuous with the rhizome and extends downward, producing a number of irregular branches.

The commercial drug may be described as follows: Nearly entire, cylindrical, very slightly tapering, 10 to 20 centimetres long, 4 to 8 millimetres in diameter; externally, grayish brown, light brown or purplish brown, slightly annulate in the upper portion, with occasional V-shaped stem scars, somewhat wrinkled longitudinally, or furrowed and sometimes slightly spirally twisted; fracture short, fibrous; internally, bark less than 1 millimetre in thickness, wood thick and composed of alternate light yellowish and black wedges; the rhizome with a circular pith; odor faint, aromatic; taste sweetish, followed by an acrid and tingling sensation resembling that of aconite but lacking the persistency and numbing qualities of the latter.

MICROSCOPICAL STRUCTURE.

The outer portion of the rhizome and root (Fig. 1) consists of two to four layers of more or less tabular cork cells with somewhat thickened yellowish suberized walls, the cells being frequently filled with more or less spherical globules of a substance which may become changed to a granular form. Beneath these outer layers of cork occur six to eight rows of tangentially elongated cells with more or less thickened walls, which are usually rich in cytoplasm, and in which is frequently found a distinct nucleus. In among these cells also occur some intercellular (schizogenous) oil and resin cavities or reservoirs (Figs. 1, 4 and 5). Beneath this second layer occur from twelve to twenty rows of parenchyma cells of varying shape, among which are large intercellular oil reservoirs and numerous small stone cells (Figs. 1, 2 and 3). These stone cells are usually more or less elongated, and frequently ten to twenty times as long as they are wide. They are of considerable interest by reason of the fact that in the intercellular spaces and in some of the adjoining cells, occur blackish, carbon-like, resinous masses

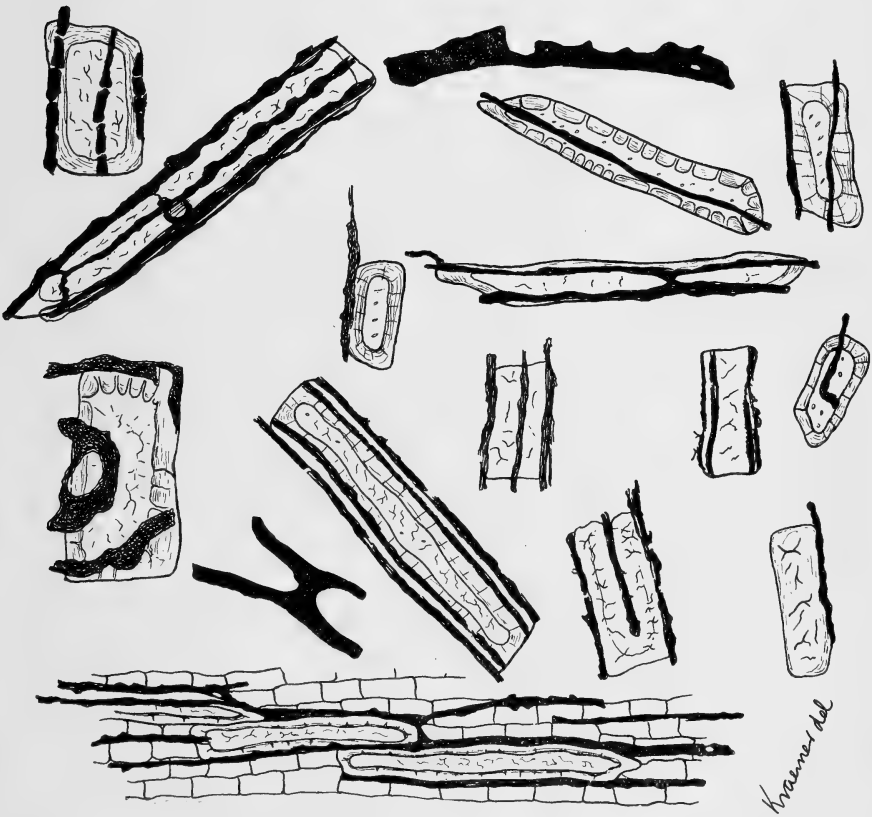
FIG. 1.



Echinacea; *A*, cross section of outer layers of root, showing cork (*c*) and hypodermis (*h*), *B*, cross section of cortex showing parenchyma (*p*), sphero crystals of inulin (*i*), and stone or sclerotic cells, and oleoresin reservoirs or canals (*o*). *C*, cross section of portion of fibro-vascular bundle showing leptome or sieve (*l*), cambium, (*m*), trachea or vessels (*t*), oleoresin reservoirs (*o*), stone cells (*s*), parenchyma (*p*) and inulin crystals (*i*). *D*, cross section near endodermis showing endodermal cells with suberized radial walls or Casparyan spots (*e*), endodermal resin canal (*o*), and parenchyma (*p*). *E*, cross section of underground stem or rhizome showing a group of bast fibres (*b*), leptome or sieve (*l*), and parenchyma (*p*). *F*, a sclerotic or stone cell. *G*, parenchyma with sphero crystals of inulin adhering to the walls. *H*, longitudinal section showing various forms of trachea or vessels; *d*, double spiral; *a*, annular; *r*, with simple pores; *p*, adjoining parenchyma.

which will be referred to in some detail later (Figs. 2 and 3). In the rhizome there is also included in this layer somewhat irregular tangentially elongated groups of bast fibres (Fig. 1, E), which give a strong reaction for lignin with phloroglucin. The walls of these fibres are not only lignified but are frequently very thick and almost transparent, very finely laminated and marked with a few simple

FIG. 2.



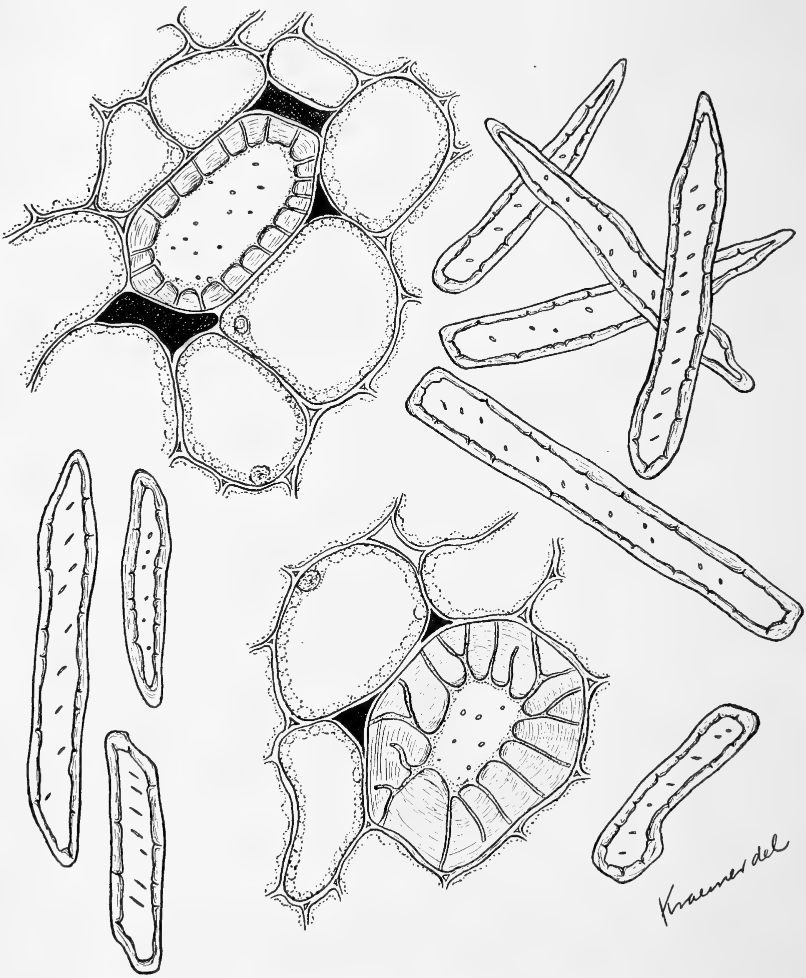
Stone cells showing the distribution of the black intercellular substance.

pores, which are more apparent when any of the ordinary reagents are employed.

The leptome or sieve extends in rays of varying width from the cambium to the outer bark, being bounded in the case of the rhizome by the bast fibres. In between these radial rows of sieve the tissue for the most part is parenchymatic and contains considerable inulin,

and the cells are interspersed with groups of from one to three of the characteristic stone cells already referred to, the groups being somewhat circularly disposed. The cambium zone is distinct, con-

Fig. 3.

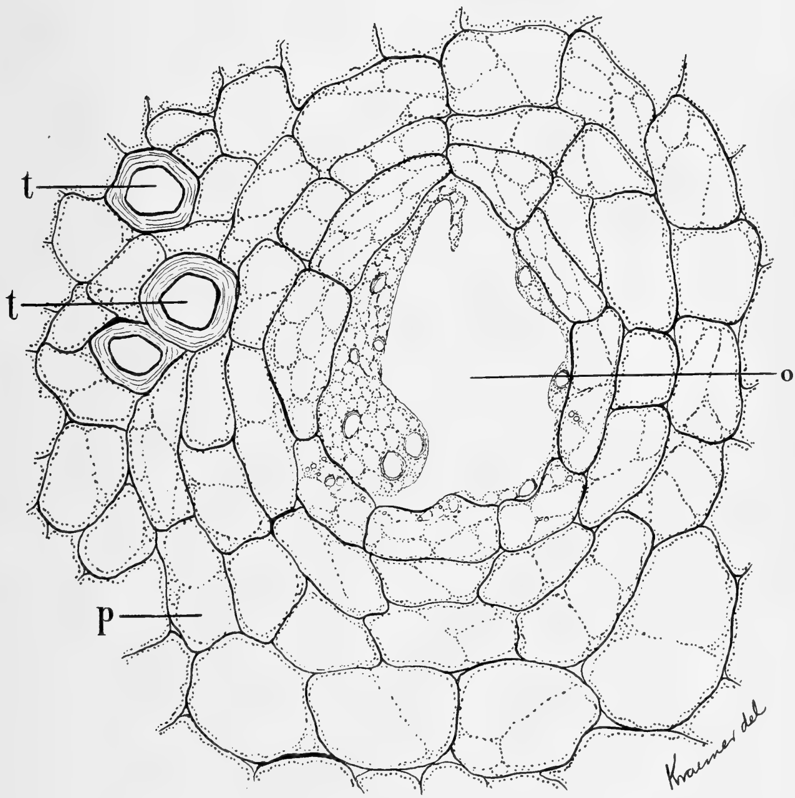


Cross and longitudinal sections showing the different forms of stone cells.

sisting of several rows of thin-walled cells. The xylem occurs in rays made up of small interrupted groups of tracheæ which are separated by wood parenchyma. The tracheæ are from eight to ten times as long as they are wide, the walls for the most part being

marked with simple slit-like pores, although annular and reticulate markings also occur. In between the xylem rays occur broad wedges consisting of from ten to twenty radial rows of parenchyma cells that are not of the type of medullary rays. Scattered among these cells are intercellular oil and resin reservoirs and more or less elongated stone cells similar to those already referred to. In

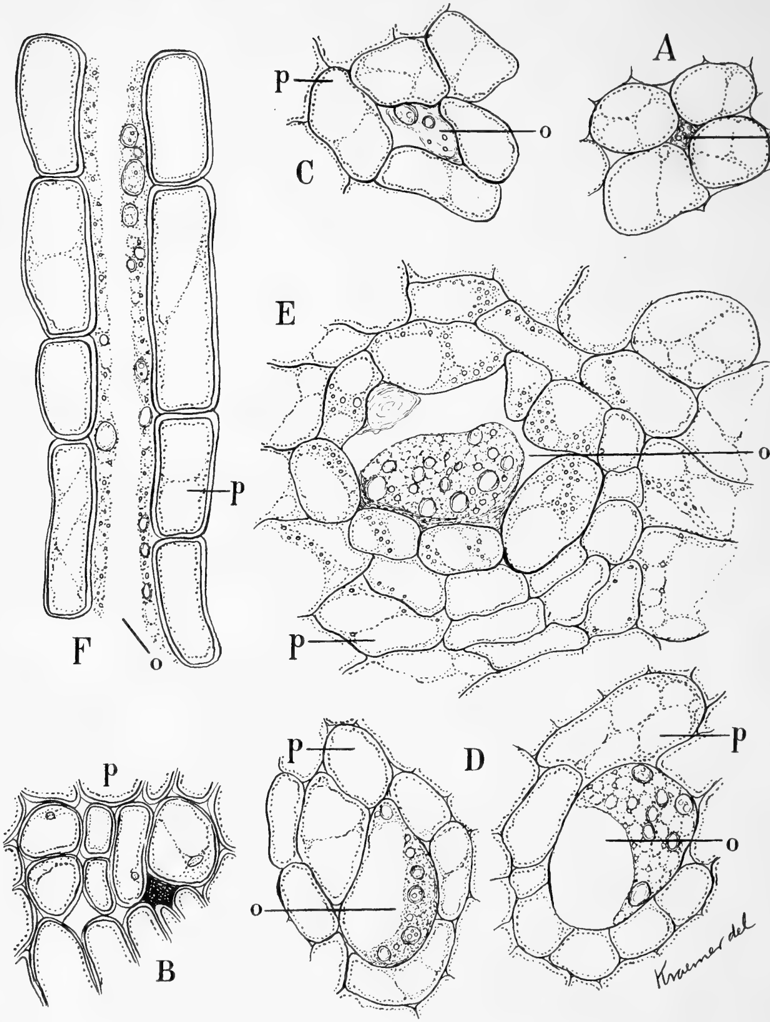
FIG. 4.



Cross section of root showing a large oleoresin canal (*o*), tracheæ or vessels (*t*), and parenchyma (*p*).

the xylem rays true wood fibres are also associated with the tracheæ in certain specimens collected in Tennessee and Missouri. The wood fibres are readily distinguished from the stone cells by reason of their position, more uniform outline and attenuated ends. In very young roots, in which the primary structure is still unchanged, the fibrovascular strand is of the triarch type.

Fig. 5.



Section showing development of oleoresin canals or reservoirs (*a*, *b*, *c*, *d* and *e*); *o*, oleoresin canals; *p*, parenchyma. *F*, longitudinal section showing an elongated secretory cell between the rows of parenchyma in the cortex.

INTERCELLULAR SUBSTANCE.

The Compositæ are usually divided for certain anatomical reasons, as well as for morphological differences, into two principal groups. In the one, viz., the Tubulifloræ, occur oils and resins, either in intercellular canals or secretory cavities. In the other,

namely, the Ligulifloræ, the oils and resins are replaced by laticiferous tubes or vessels. In only one genus (*Gundelia*) of the Tubulifloræ are laticiferous tubes present, and while the root of this plant apparently contains resin canals, these are wanting in the leaves and stems. Again, in only one genus (*Scolymus*) of the Ligulifloræ are oil canals present, as well as latex tubes (see DeBary, p. 137; and Engler and Prantl, p. 351).

The oleoresinous canals or reservoirs (Figs. 1, 4 and 5) found in *Brauneria pallida* are of the general type occurring in the Tubulifloræ. They are quite numerous and in some instances quite large, and are found in both the wood and the bark. The contents are of a light yellowish, amber-like color and of an oily or resinous consistence. There appears to be no relationship between the substance found in these oleo-resinous canals and the black substance present in most of the intercellular areas around the stone-cells. This latter substance is of a nearly uniform black color, insoluble in both sulphuric and nitric acids, and the ordinary solvents, such as alcohol, acetone and petroleum ether, etc. In longitudinal section, or upon treating the drug with Schultze's Macerating Fluid, it is found that this substance forms a somewhat coarse network, the material from a number of intercellular areas being more or less connected and the network resembling a septate latex tissue. Beyond this appearance there is no resemblance between the network of black intercellular substance and true laticiferous tissue. In some of the parenchyma cells of both the bark and the wood there may occur a black substance resembling this intercellular substance, which would seem to be in the nature of an excretion from some of these cells.

It should be stated, however, that in some of the longitudinal sections there was observed in the cortical tissue a number of elongated areas containing an emulsion of a yellowish oily or resinous substance. It could not be determined with certainty whether these were in the nature of elongated secretory cells or merely intercellular spaces into which had been secreted the oleo-resinous material. There are a number of facts which would seem to lead to the inference that they are probably in the nature of elongated secretory cells.

Some time ago Moser published an article on Echinacea and a Spurious Root, that appeared in the fall of 1909 (*A.J.Ph.*, 1910, p. 224). As he did not have an opportunity of studying authentic

material, or that derived from plants which were identified, his statements and description will need to be modified in order to accord with the facts here presented. Furthermore, the spurious drug described by him was really that of authentic material, as I have several specimens of the root from herbarium material of *Brauneria pallida* collected in Missouri and Tennessee, which are similar to the drug examined by him. Of course it is quite likely that other species of *Rudbeckia* or *Brauneria* may have some of the fundamental characteristics of *Brauneria pallida*, the root of which together with the underground stem or rhizome, is the source of the drug known as Echinacea.

FLUID EXTRACT OF ECHINACEA.[1]

By George M. Beringer.

Echinacea is one of the vegetable drugs that, in recent years, has attracted considerable attention in the medical profession, and appears to merit more extended study. By some its virtues are highly extolled, by others it is considered worthless. It is, however, to be noted that the condemnation is largely based upon the fact that certain chemists who made an examination of the drug had failed to isolate the active principle. We need not be surprised at this as the chemistry of many of the compositæ has been but little studied and very few alkaloidal or glucosidal principles have been isolated from drugs of this plant family.

The aromatic principles present in Echinacea are probably the source of its therapeutic action. The root has a characteristic aromatic, sharp and pungent taste, reminding one of the peculiar pungency of certain umbelliferous drugs such as lovage and angelica. It leaves a warm and tingling sensation in the mouth and is sufficiently irritant to produce a prickling sensation and a slight blistering effect on the mucous surfaces of the lips. This pungency and blistering effect is even more marked in alcoholic or hydro-alcoholic extracts.

Echinacea is a plant indigenous to the western plains of the United States. The professional use was preceded many years by

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[1] Read before the New Jersey Pharmaceutical Association at Asbury Park, N. J., June 14, 1911.

that of certain aboriginal tribes. The Sioux Indians are said to have used it as a remedy in snake bites, insect stings, and in the healing of wounds. Its use in medical practice, to-day, is very much along the same lines. It is considered as a mild counter-irritant, stimulant and antiseptic, and as a remedy useful in blood disorders, typhus and meningitis and likewise recommended externally in the treatment of carbuncles, hæmorrhoids, wounds and impotency.

The fluid extract is the form in which the drug is commonly exhibited and its use certainly merits recognition and the fixing of an official standard therefor. It is proposed to introduce a formula for the fluid extract in the National Formulary. In connection with the work of revision of this legal authority, the writer has experimented with various formulas suggested for this preparation.

The views of manufacturers consulted showed a wide variation. While one recommended diluted alcohol for the menstruum another preferred 80 per cent. alcohol, and the recommendations of others fell between these extremes. This difference in the opinions of manufacturers accounts for the difference existing in the commercial products and shows the necessity for an official standard.

My experiments lead me to the conclusion that a menstruum weaker in alcohol than alcohol 2 volumes, water 1 volume, will not extract the drug. A menstruum of that strength appears to make a fluid extract of good body and color and taste, but it is not quite clear and some separation takes place. A menstruum of alcohol 3 volumes, water 1 volume, is a decided improvement over the weaker alcohol and shows only a very slight tendency to separation. The best result in my judgment is obtained with a menstruum of alcohol 4 volumes, water 1 volume, and is recommended for this fluid extract. To increase the alcohol beyond this strength seems unnecessary and yields a product lacking in body and no more aromatic than the menstruum preferred.

THE FIFTH REVISION OF THE GERMAN PHARMACOPŒIA.[1]

By George M. Beringer.

The appearance of a new edition of the German Pharmacopœia is always an important event in the history of pharmacy. The fifth revision of the Deutsches Arzneibuch has been published during the past year and became effective and the authority in the German Empire on January 1, 1911. Its publication on the eve of the Ninth Revision of the United States Pharmacopœia, adds materially to its importance.

Owing to the great number of our inhabitants who are of German birth or descent and also to the numerous American physicians who have been students in the German medical schools, the practice of medicine and pharmacy in this country, in many matters, largely follows the German.

The present revision marks the progress of professional pharmacy in Germany since 1900, when the fourth revision was published. Many of its departures are meritorious advances and will have marked influence on other pharmacopœial revisions, and its pronouncements are worthy of our careful study. I have no doubt that they foreshadow some of the principles and standards that will be adopted in the revision of the U.S.P. On the other hand, one is impressed by the fact that the U.S.P., 8th revision, was undoubtedly the model for some of the noteworthy changes in the latest German revision.

The object of the present communication is to direct attention to the more important features of the revision as the limitation of our meeting necessarily precludes a detailed review of the book.

As in the previous revisions it follows the custom of stating formulas, when not dosage forms, in parts by weight, even in the formulas for fluid extracts, and the finished products are given as 4, 5, 9, 10, 20, 50, 100 or 500, etc., parts. The uniformity of the U.S.P. in this respect is lacking in the German.

One of the noted departures in this revision is the style of giving formulas. The U.S.P. method of stating all the ingredients and quantities in the beginning of the formula and then following with

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[1] Read before the New Jersey Pharmaceutical Association at Asbury Park, N. J., June 14, 1911.

directions is adopted in place of the method of the previous revisions wherein each item was preceded by the amount printed in words and the process was elaborated throughout the formula.

In the monographs on drugs and chemical products the style of treatment more closely simulates that of the U.S.P. VIII. The purity rubric has been adopted and is quite generally given in the chemical products. Here, however, one notes a lack of uniformity. For examples, Potassium bromide " must contain not less than 98.7 per cent. of pure KBr " (U.S.P., 97 per cent.) and Potassium carbonate " in the neighborhood of 95 per cent. pure K_2CO_3 " (U.S.P., 98 per cent.), but the monographs on Potassium Iodide, Potassium Bicarbonate, and Potassium Nitrate, as well as those of other salts, lack entirely such statements of the purity requirements. This shows a lack of co-ordination of the work of the revision or a failure to adhere systematically to what appears to have been intended as one of the advanced thoughts to be adopted in the work.

The purity rubric is extended to many of the drugs and even to some of the galenicals. Here the method of stating the purity requirement at the very beginning, preceding even the definition of the drug or the process of the preparation, does not appeal to the writer as an improvement over the U.S.P. method of including the alkaloidal standard as part of the definition. It strikes us as odd to see as the initial statement in Cantharides " contains not less than 0.8 per cent. cantharidin," and in Cinchona " contains not less than 6.5 per cent. alkaloid, consisting of a mixture of quinine and cinchonine," or in oil of Lavender " contains not less than 29.3 per cent. Linalylacetate," and in Extract of Hyoscyamus " contains 0.5 per cent. Hyoscyamine " (U.S.P., 0.3 per cent. mydriatic alkaloids.

In the official titles, many of the old time-honored Latinized vernacular names are retained and such mediæval titles as " Borax," " Cerussa," " Lithargyrum," " Minium," still appear in this twentieth century revision.

The German method of spelling Latinized chemical names is retained in the official titles. As examples, Baryum chloratum with the German synonym as Baryum chlorid, Kalium chloricum with Kalium chlorat as synonym and Morphinum hydrochloricum with morphin hydrochlorid as the German. This has always been confusing to the English-speaking nations.

The method of classifying titles so that the official barks, leaves,

flowers, roots, rhizomes, etc., appear together, is retained, and in each drug the title indicates the part of the plant official. A few changes in titles are specially noticeable. Folia Hyoscyami replaces Herba Hyoscyami and Rhizoma Rhei, the former Radix Rhei; Formaldehydum solutum is changed to Formaldehyd solutus, and Paraldehyd now appears in place of "Paraldehydum." A noteworthy change in title as well as in composition is Lanolinum, which now becomes a mixture of wool fat 15, water 5, and liquid paraffin 3 parts, with "water containing wool fat" as the synonym and the old title Adeps Lanæ cum Aqua, for a mixture of wool fat 75 and water 25, is dismissed. The Unguentum Adipis Lanæ is also dismissed, the evident intent being that the new Lanolin shall serve for both of these old formulas.

The German Pharmacopœia recognizes the fact that the commercial chemicals sold for many purposes are legitimate subjects for its consideration and standardizing. We find such articles as crude sulphuric acid, crude copper sulphate, crude iron sulphate, crude potassium carbonate, and crude zinc oxide treated in suitable monographs.

Nor in the consideration of vegetable drugs does the German Pharmacopœia restrict its standards to the ingredients of physicians' prescriptions. It recognizes the necessity for proper definition for such common drugs as lavender flowers, chamomile, elder blossoms, mullein, coltsfoot, walnut leaves, sage and foenugreek which, while only occasionally dispensed on physicians' prescriptions, are largely used in domestic practice and become not an inconsiderable portion of the dealings of the druggist.

The International List of Atomic weights for 1910 is adopted as the basis for the chemical formulas, molecular weights, and the analytical calculations. This is the first revision of the German Pharmacopœia in which chemical formulas are given. Empirical formulas are tabooed and throughout structural formulas are used. While in many places simple structural formulas, like those of the U.S.P. VIII, are given, in others more elaborate formulas are presented. This is shown in the extreme in Theophyllin or Theocin where a modified graphic structural formula is given and a definition is omitted. This laxity of official definition is shown in a number of the monographs especially those describing organic chemicals and alkaloids.

The introduction of formulas and processes for the manufacture

of such chemicals as the nitrate, subgallate, subnitrate and subsalicylate of bismuth, calcium phosphate, iron and quinine citrate, quinine tannate, etc., seems strange to us in the light of present-day experience and economic conditions. Modern division of labor has rendered such manufacture unprofitable for the pharmacist, even if he should be equipped with the facilities to undertake it.

A very commendable feature of this revision is the introductory chapter devoted to official methods to be followed in the making of such determinations, as melting point, congealing point, boiling point, ash, acid number, saponification value, ester value, iodine absorption, etc.

Specific gravity, unless otherwise stated for special reasons, is taken at 15° C. compared with distilled water at 15° C. The U.S.P. VIII has not been followed by a single pharmacopœia nor by the U. S. Government departments in the adoption of 25° C. as the temperature for such determinations and the writer personally doubts if we really assumed "an advanced" position in adopting 25° C. or if we are now justified in retaining it alone against all pharmacopœial and other scientific authorities.

Polariscope readings are by sodium light at a temperature of 20° C. unless otherwise stated. In essential oils the figures are for reading with 100 mm. tube.

Microscopic measurements are stated in microns the μ being equal to 1/1000 mm.

The degree of fineness of drugs is indicated by a scale of numbers varying from No. 1 to No. 6, No. 1 being coarsely comminuted drugs passing through a sieve whose meshes are 4 mm. apart, and No. 6 being finely pulverized drugs passing through a sieve whose meshes are about 0.15 mm. apart.

For counting drops the normal drop counter of the Brussels Conference is adopted, and the method of stating doses is retained as in the previous revision, namely, the largest single dose and the largest daily dose.

Possibly the greatest advance is shown in the monographs treating of the organic drugs. Here we note first the innovation of giving the botanical authorities for the plant names, and these are quite generally the more recently accepted authorities. Secondly, and most praiseworthy, is the microscopic descriptions so generally included. These evidence the great advances made in the science of pharmacognosy since the last revision. Another commendable feat-

ure is the statement of ash content quite generally given. The method of stating the amount of alcohol soluble content in such drugs as asafetida and benzoin is to be commended as clear and worthy of copying in the U.S.P. Our Pharmacopœia directs that benzoin be "almost wholly soluble in 5 parts of warm alcohol." The German Pharmacopœia that "on thorough extraction with boiling alcohol the residue on drying must not exceed 5 per cent. of the benzoin."

The Ph. Gr. requires for asafetida that "on thoroughly extracting with boiling alcohol, and drying the residue at 100° C. it should not exceed 50 per cent. of the amount taken. The ash is limited to "not over 15 per cent.," the U.S.P. states "not less than 50 per cent. should dissolve in alcohol," and the ash limit is not more than 10 per cent.

Assay processes are greatly extended and improved and new ones are added for a great many articles not heretofore assayed. As examples of the extent to which assaying has been extended may be mentioned mustard paper and pomegranate bark. The selection of the articles assayed, however, is not readily understood. As, for example, assays are given for oils of cinnamon, lavender, santal and mustard, the latter being the synthetic oil, yet no assays are given for oils of anise, lemon, peppermint or rosemary equally important and assayable. In the alkaloidal assays where the alkaloid is estimated by titration iodeosin is the indicator commonly directed. Where assay processes are not available, not infrequently identification tests are given. As example, Bornträger's reaction for oxymethylanthroquinones is given as a characteristic test for the fluid extracts of frangula and cascara sagrada.

The attempt to follow the protocol of the Brussels International Conference is evidenced not only in the adoption of the Normal Drop Counter recommended but also in the adoption of many of the formulas and standards for potent drugs. Such adoption is indicated by a subtitle in Latin with P. I. appended. However, there are a number of instances where deviation in menstruum from the international 70 per cent. alcohol is made, yet the P. I. is appended. Example, Tinctura Cantharidis and Tinctura Iodi in which alcohol is directed. In a number of other cases where some deviation has been allowed the P. I. is not appended as, for example, Tincture of Aconite, although 10 per cent. drug is not indicated as international probably because no assay is given. Nux Vomica and

Strophanthus are not marked P. I. yet the tinctures made therefrom are both marked P. I.

To Tincture of Colchicum is appended the instruction that when Vinum Colchici is directed the tincture is to be given therefor and to Tincture of Ipecac is a similar instruction given that when Vinum Ipecacuanhæ is ordered the tincture is to be dispensed. The wisdom of such modification of physicians' orders is not above question and also the consistency of an agreement that "a potent medicament should not be prepared in the form of a medicinal wine" and then the same convention immediately proceeded to adopt an international standard for wine of antimony. Is there any reason why Vinum Ipecacuanhæ should be eliminated from medical practice and "Vinum Stibiatum" retained?

The admissions to the official list are interesting and while some are but little known or used in the United States others are extensively used. In the selection of pharmacopœial titles the Germans are not handicapped by product patents and trade-mark laws, and if the chemical name is too lengthy or not suitable for an official title they simply take the common or trade name, even if considered proprietary, and adopt it as the official title. This is shown in the present revision by the adoption of such titles as Stovaine and of Anæsthesin for para-amino-benzoic-ethylester. Even when the chemical name is Latinized as the official title the common or trade-mark name is given as an official synonym. Thus under Acidum Acetyl-salicylicum, Aspirin is so given and under Acidum diacetylbarbituricum, veronal is stated as the synonym. Among the other more important admissions we note dionin, heroin, colloidal silver, silver proteinate, beta eucaine, lactophenin, arsacetin, atoxyl, novacaine, phenolphthalein, tropacocaine hydrochloride, theocin synthetic and suprarenin hydrochloride which latter may be either the natural from the gland or the synthetic which is of doubtful value. Some of the additions such as gallic acid, guaiacol carbonate, hexamethylene tetramine, solution of hydrogen peroxide and cascara sagrada are so well established in American practice that we think our German friends at least a decade slow in their adoption. Concerning cascara an inconsistency in the title is shown; the drug is recognized as "Cortex Rhamni Purshianæ," yet the fluid extract is entitled "Extractum Cascaræ Sagradæ fluidum."

Collemplastrum is a new title for the rubber adhesive plasters and two formulas are given collemplastrum adhæsivum and col-

lemplastrum zinci, for the two popular plasters, surgeons adhesive plain and with zinc oxide. Their formulas contain caoutchouc, wool fat and copaiba balsam, with powdered orris root as a filler, and are well worth experimenting with as a substitute for our official adhesive plaster that is never made.

Peanut oil is introduced and is directed as an ingredient in some of the plasters, ointments and liniments, but it is to be noted that for camphorated oil the German Pharmacopœia still adheres to olive oil.

Among the articles dismissed we note hydrobromic acid, dried egg albumin, tar water, ferric chloride, jaborandi, poppy capsules, vanilla, solution ammonium acetate, syrup of poppy, wines of colchicum and ipecac.

The galenical preparations are classified into numerous distinctive classes and each class is headed by a short descriptive paragraph or chapter setting forth its definition and such general instructions as are appropriate.

The German still lovingly adheres to his idol, maceration, and percolation, as yet, receives but scant consideration in his pharmacopœia. While percolation is directed in a few formulas such as the fluid extracts, where the rate of flow is fixed at 30 drops per minute, yet in other important extractions such, as for example, Extract of Nux Vomica, maceration and expression is directed.

The requirements or some of the important articles are briefly given so as to be compared with those official in the U.S.P.

Alcohol is 91.29 to 90.09 per cent. by volume.

Diluted Alcohol is 69–68 per cent. by volume, thus corresponding closely with the 70 per cent. alcohol recommended by the Brussels Conference as a universal menstruum for tinctures of potent remedies.

Acid Benzoic is the sublimed and from Siam Benzoin, and tests are given to detect the synthetic. The U.S.P. recognizes both with preference for the synthetic.

Acidum Carbolicum is still retained as the title for "Phenol."

Hydrochloric Acid remains "about 25 per cent. HCl" and the diluted 12.5 per cent.

Phosphoric Acid remains 25 per cent. H_3Po_4; the U.S.P. is 85 per cent.

Aloe is restricted to the inspissated juice of the leaves of "African species of Aloe" with omission of the exact botanical source.

Ammonium Carbonate like the U.S.P. is the academic statement rarely if ever found in commerce.

Cantharides is required to contain 0.8 per cent. of Cantharidin. The assay process has been improved by recrystallizing the product from Acetone, but it still does not yield a colorless and pure product.

Sulphuric Acid is 94 to 98 per cent. H_2SO_4, the crude 91 per cent. and the diluted 15.6 to 16.3 per cent.

Capsules are described as of two forms, the platter or cup-shaped made of wheat flour or wheat starch, and the hollow gelatin capsule.

Catechu is retained; no Gambir for the Germans.

Cinchona is restricted to the Bark of Cinchona Suiccirubra Pavon.

Quinine Sulphate: The chemical formula is given as containing 8 molecules of water. The U.S.P., while giving the formula as $7H_2O$, in the text allows a loss in drying, "indicating not more than 8 molecules of water."

Cinnamon: The Ceylon bark replaces the Chinese and the oil of Ceylon Cinnamon is now the German official oil of cinnamon.

Fluidextracts: But four new ones have been added, namely, cascara, cinchona, granatum and simaruba. The Cinchona contains 17 parts of Diluted Hydrochloric Acid in 100 and is essentially the formula of the British Pharmacopœia.

Sassafras is the wood of the root.

Solution of Iron Albuminate: Fresh hen's egg albumin replaces the dried of the previous edition. The variability of the commercial dried albumin and disagreeable odor possessed by many samples necessitated this change.

Liquor potassii hydroxidi and Liquor sodii hydroxydi are both "about 15 per cent." while the U.S.P. are only about 5 per cent.

Magnesium Carbonate: Two chemical formulas are given showing varying mixtures of magnesium carbonate and hydroxide, the one with 3 molecules of H_2O and the other with 4. The U.S.P. gives the latter formula but with 5 molecules of water. Probably both authorities give academic formulas that do not describe the trade article.

Opium is required to contain "not less than 12 per cent. of morphine after drying at 60° C." It would be rather difficult to dry a substance like opium uniformly at that temperature.

Powdered Opium is required to contain 10 per cent. of anhydrous morphine. The U.S.P. standard 12 to 12.5 of *crystallized* morphine varies but slightly from the international agreement.

Pill of Aloes and Iron, very similar to the U.S.P. formula, is retained.

Sarsaparilla is continued as the " Honduras " variety.

Taraxacum is the " root with herb " collected in the spring before flowering.

Artificial Carlsbad Salt remains in the German Pharmacopœia. This is an N.F. preparation that has been severely criticized because a factitious product.

Sapo Kalinus remains quite properly a linseed oil soft soap.

Scopolamine hydrobromide is the lævarotory " hyoscine," and the latter title is not given.

Ergot is directed to be kept for not more than one year, and not kept in the powder form, but powdered as needed.

Strophanthus: Seed of S. kombe Oliver only, but in the tincture the protocol is blindly followed despite its error, and a 10 per cent. drug tincture is made with 68 per cent. alcohol and the seed not previously defatted.

Nux Vomica: The standard is 2.5 per cent. mixed alkaloids strychnine and brucine, of which it is assumed that a little more than half is strychnine.

Serum Antidiphthericum: Here the serum antitoxin and the dried antitoxin are recognized but the concentrated globulin form which is so extensively used in the U. S. is not mentioned.

Physiological Salt Solution is given as Sodium Chloride 8. Sodium Carbonate 0.15, water 991.85 parts, filtered and sterilized.

Spirit of Lavender is directed to be made by macerating for 24 hours 1 part lavender flowers and alcohol 3 and then distil off by the water bath 4 parts. This is an impossible formula and evidently there has been an omission of the 3 parts water directed to be added in the 4th Revision.

Tincture of Ipecac: A new introduction to meet the theoretical user of the P. I.

Each formula is accompanied by a description of the product and not infrequently this gives in addition to the color, consistence, taste, etc., also the specific gravity and the percentage of extractive and ash, and any distinctive characteristic reaction or test.

Several of the important features of this revision are contained in the chapters of the appendix. The first being the list of elements and atomic weights. The second is the chapter on reagents and volumetric solutions. The third chapter is a list of reagents and

volumetric solutions for medico-chemical examinations. This is one of the most commendable features of this revision and places in a compact schedule these reagents and tests and should prove a valuable aid to the busy practitioner or pharmacist. The classification here is according to the subjects of investigation, the first sub-heading being the reagents for urine analysis, and this is sub-divided under paragraph headings directions for albumin, for sugar, for pentoses, for acetone, for acetic acid, for urobilin, for urobilinogen, for gall coloring matters, for indican, for carrying out the diazo reaction, for iodine, for salicylic acid and for blood. The second classification is for the investigation of stomach contents. The third for the examination of blood. The fourth is for the examination for bacteria and protozoa, and here formulas are given for the necessary stains and reagents and the standards are here given for the cedar oil, Canada balsam and xylol suitable for microscopic investigations.

Another chapter of the appendix is a table of specific gravities of the official liquids at temperatures from 12° to 25°. Although doses are given with each monograph or formula in the body of the book, a table of maximum doses for adults is given in the appendix. Another table is devoted to a list of the deadly poisons that must be kept under lock and dispensed with great caution. Still another table is devoted to other less poisonous or dangerous medicaments that one should beware of. An extensive list of synonyms and less used names is one of the important tables included in the appendix.

THE LACTIC ACID ESTER OF SANTALOL AND OTHER SANTALOL COMPOUNDS.[1]

By Frédéric S. Mason, B.Sc., Ph.G., M.D., New York.

I should have liked to have introduced the subject of my paper by a short review of the history of sandalwood and its oil, for with ambergris and musk, sandalwood is one of those natural products used from very remote ages in perfumery and medicine. I have been interested in sandalwood for over twenty-five years, having been one of the first to make an investigation of the sources of supply in India, Malaysia, Timor and Western Australia, which countries I visited on two occasions for the specific purpose of determining the cause of the variations observed in the laboratory,

[1] Read before the New York section of Am. Chemical Society, 5th May, 1911.

when examining the oils obtained from wood bought on the London market. In recent years, a peculiar malady called in Mysore "spike disease" attacked the sandalwood; parasitic roots of other trees attaching themselves underground to the sandalwood roots even at from one to one hundred feet distance. This disease at one time bid fair to exterminate these valuable trees, but the Mysore government, which derives an important revenue from this source, is now engaged in heroic efforts to save them.

My time, however, being limited to twenty minutes, I refrain from enlarging on this subject and must refer those who are interested to the contributions to materia medica which I have published from time to time in the *Pharmaceutical Journal* of Great Britain, and more recently in the American edition of the *Tribune Medicale* of November, 1909.

It is now recognized that the most valuable oil is obtained from the heart wood of the true *Santalum album* growing on the highlands of Mysore in Southern India, and it is with this product that I am dealing in the present paper.

In confirmation of what I have already published on sandalwood oil distilled in India, I will quote from Schimmel's Semi-annual Report of October, 1910, since it confirms much that I have already written on the Sandalwood of Mysore, although reference is here made to an outlying territory: "The distillation of sandalwood oil appears to be an ancient industry in Southern Kanara, especially in the district of Udipi, but it is steadily declining. Natives from Udipi attend the auctions in Mysore and Coorg every year, and attract attention by their bids, which are often extravagantly high, especially for Coorg wood. But not all the wood bought by these dealers is distilled by them: a portion of it they resell to Bombay. It is said that the distillers also use smuggled wood (sandalwood being a monopoly of the State of Mysore), besides which sandalwood trees may occur here and there in the district of Kanara.

"The oil industry is centred principally in the district northeast of Karkul up to the foot of the Ghats.

"For distilling purposes, the wood is cut into chips and placed in the still. Water is then added and the distillation of the same charge is continued uninterruptedly day and night for a whole month. Fresh supplies of water, consisting of the luke-warm water taken from the cooling vessel, are poured into the still about 15 times every 24 hours. The oil-yield is said to be as follows:

Roots	about	4.34%
Jugpokals	"	3.47%
Ain Chiltas	"	2.60%

"The oil is partly brought to market at Udipi and partly at Mangalore. Almost all the oil is shipped by steamer to Bombay, whence it is exported to the Persian Gulf and to China.

"It hardly needs to be pointed out that under the primitive conditions of distillation which have been described, it is impossible to obtain any really good sandalwood oil. Owing to the prolonged duration of the distilling process, decomposition-products must necessarily be formed, which must injuriously affect the quality of the oil and be equally unfavorable to its color and odor."

Santalol, in two isomeric forms, occurs as the alcohol of the East India sandalwood oil, and is recognized by all therapeutists as the chief active component of this oil. The older pharmacopœias have been content to establish a standard based on the specific gravity and its solubility in alcohol, but the present U.S.P. requires 90% of santalol and states that the oil is lævogyrate—its angle of rotation should not be less than $-16°$ nor more than $-20°$ in 100 Mm. tube, at a temperature of 25° C. This differentiates the true oil of the *Santalum album* (N.O. Santalaceæ) from those derived from species of sandalwood or adulterated with cedar and other spurious oils.

Chapoteaut, in 1879, read a paper before the Paris Societé de Chimie, and was the first to call attention to the fact that sandalwood oil was composed chiefly of alcohols, from which he was able to make a series of esters with appropriate acid anhydrides. The empirical formula of the santalol he then referred to, he determined to be $C_{15}H_{26}O$. He also isolated another body, to which he ascribed the formula $C_{15}H_{24}O$, and these findings were verified by Chapman & Burgess (*Proceedings of the Chemical Society*, London). Parry followed up Chapoteaut's work some years later, and Continental chemists have since shown that the pure oil is chiefly composed of a mixture of the santalols together with two isomeric sesquiterpene alcohols. Guerbet speaks of an alpha- and beta-santalene, which both combine slowly with glacial acetic acid when heated in sealed tubes. The hydrochlorides of santalol $C_{15}H_{24}2$ HCL, have an optical rotation in an opposite direction to the original sesquiterpenes, that of the alpha-santalene hydrochloride being 6° 1′, and that of beta-santalene hydrochloride 8°. Alpha-santalene gives only one crystal-

line nitrosochloride at 122° C., and is insoluble in alcohol. Beta-santalene gives two isomeric nitrosochlorides, both of which are soluble in alcohol. The two santalols, isolated together from other constituents of the oil as phthalic esters, can only be separated from each other after saponification by fractional distillation under reduced pressure. Thus obtained, the alpha-santalol boils at 300°–301° C. (as pointed out by Chapoteaut in his first paper of this subject), has a density of 0.9854 at zero centigrade and a rotation of — 1° 20′. Beta-santalol boils at 309°–310° C., and has a density of 0.9868 at 0° C. and the rotation is — 56°. Dehydrating agents, such as acid potassium sulphate or phosphoric anhydride, remove a molecule of water, converting them into their respective isosantalenes $C_{15}H_{24}$. Alpha-isosantalene boils at 259°–260° C., so that the alpha and beta compounds approach very nearly to the essences of copaiba and cedar. Hugo and Soden have also given considerable time to the examination of sandalwood oil. F. Muller claims to have isolated a new terpene C_9H_{14}, which he calls santene. This has a Sp. gr. of 0.871, and boils between 139°–140°. It forms two polymeric crystalline nitrosochlorides, one blue and the other colorless. It also gives a solid hydrochloride melting at 80° C., thus conforming with the reactions of other terpenes. This terpene is probably derived during distillation from teresantalic acid, since when that acid is heated under a reflux condenser, CO_2 is found to be given off and on distilling, santene is obtained. Muller also found a ketone, santalone $C_{11}H_{16}O$, boiling at 214°–215° C., isomeric with jasmone.

To summarize, the following definite compounds have been isolated from sandalwood oil: (per kilogr.)

Santalenes "a" and "b"	60
Santalols "a" and "b"	800
Santalal	30
Acids in the state of esters (formic, acetic, santalic, teresantalic)	30
Undetermined strongly odorous bodies boiling at 130°–220° C.	3
Undetermined products boiling about 320° C. (hydro-carbons, alcohols, ethers, resinous products)	77
	1000

From a series of examinations made by Sodan and Muller, these authorities suggest the following constants for sandalwood oil:

Specific gravity	0.975 to 0.982
Optical rotation	16° to 20°
Refraction index	Not below 1.5030
Santalol (total)	At least 90 per cent.
Esters as santalyl acetate	4 to 6.5 per cent.
Rotation of first and second fractions of 10 per cent.	Not below 16°

Sandalwood oils found on the drug markets of London and the Continent are now sold with a guarantee of 94 per cent. of santalol, but this guarantee should not be taken too seriously, since repeated examinations of various brands show that they vary between 90.9 and 93.6 per cent. of santalol with from 1.5 to 6 per cent. of the esters of santalol. Occasionally an oil is found which gives as high as 98% of santalol. These variations explain the variable specific gravity of the oils found in commerce. The U.S. Pharmacopœia gives the specific gravity as .965 to .980 at 25° C. We see, therefore, that the requirements of the U.S.P. are moderate and allow for variation in the percentage yield of santalol.

Since the santalols are responsible for the medicinal effects of sandalwood oil, it is with these definite products that we have chiefly to deal. Sandalwood oil and santalol, however, are not well tolerated by most patients, and chemists have, in recent years, attempted to form compounds with these alcohols in order to obtain less irritating esters, while retaining their beneficial medicinal effects. Many processes have been patented, the patentees claiming that santalol esters are better tolerated and less objectionable in taste, while their therapeutic activities are retained. The general principle for the production of these esters is to act on the santalol with an anhydride or by obtaining compound esters by action between a santalol halogen and an alkaline ethylate, phenylate, etc. Solid esters in fine white crystalline needles, such as the santalol ester of allophanic acid, containing 72 per cent. of santalol, have been obtained. The neutral esters of the aromatic acids, however, are the best known, and amongst the rather long list, the following have had a passing notice and are used to some extent: Santalol benzoate, salicylate, cinnamate, succinate. A phosphate has also been obtained.

As these santalol compounds are incompatible with alkalies, the

theory of their activity is based on the supposition that the alkalinity of the duodenum breaks them up, liberating nascent santalol. The therapeutic dose, however, has to be somewhat increased according to the molecular weight of the ester. These compounds of santalol are known under various trade names and need not enter into discussion here.

In considering a compound of santalol for medicinal use, we should look for one which will not interfere with the gastrointestinal digestive processes and which will be finally eliminated during metabolic changes, as santalol, Co_2 and H_2O. This I think is best realized in the lactic acid ester of santalol ($CH_3CHOHCOO$, $C_{15}H_{25}$), which represents 69.74 per cent. of pure santalol. It has the advantage of being more agreeable to the taste than sandalwood oil or santalol, it is well tolerated and can be administered in the form of capsules. Like other lactates, the lactic radical is completely consumed in the economy. It renders the urine somewhat alkaline, diminishes the overstimulation of the renal parenchyma and does not occasion the pain in the back so often complained of by patients to whom sandalwood oil is administered.

While lactic acid does not react directly with santalol, its primary and secondary anhydrides, the so-called lactid, do so under certain conditions, and a patent has been granted for the process of manufacture of the santalol lactate in the United States and England and is pending in Germany and France. In practice, this is obtained by driving off from syrupy lactic acid 25 per cent. of the compound with water, leaving the primary and secondary anhydrides, the dilactic anhydride of Pelouse, or lactid, which is solid to 25° C.

It is an advantage to use a slight excess of the lactid over and above the theoretical combining molecular weights and this leads to some difficulty in the purification of the final product, which is one of the essential points of the patent, for it is exceedingly bitter and disagreeable to the taste and can only be removed from the santalol lactate with difficulty. Primary and secondary lactic anhydrides, therefore, are placed in contact with the santalol, in the molecular proportions necessary for chemical combination and heated in a partial vacuum to a temperature not exceeding 130° C.

For therapeutic use, and for reasons of economy, it is considered unnecessary to obtain an absolutely pure santalol lactate, and in its manufacture, U.S.P. sandalwood oil containing at least 90% santalol was used, rather than pure santalol.

As the result of a number of experiments, the following was found to yield a santalol lactate of from 92 to 95% purity (according to the percentage of santalol in the sandalwood oil used) and was finally adopted:

Sandalwood oil in the following proportions (weight) 110 grams (equivalent to 100 grams santalol in the sample) and 120 grams of solid anhydrides (lactid) of lactic acid, were placed in a flask attached to a Liebig condenser. Heated in a partial vacuum to 108–110° C., a primary reaction occurs with ebullition. The temperature was then gradually raised to 125–130° Cent., when a more violent secondary reaction took place. The temperature was maintained at 130–135° C. for twelve hours. There was no distillate at this temperature. The contents of the flask were then boiled repeatedly with distilled water for several hours to remove the bitter taste of the excess of lactic anhydride present.

The product was washed with a 1% solution of $NaHCO_3$, then with 1% HCl; washed again with distilled water until it gives no opalescence with $AgNO_3$, filtered and estimated for the proportion of combined santalol and lactic acid.

THE THEORETICAL PERCENTAGE COMPOSITION OF SANTALOL LACTATE.

Santalol "A" and "B" $C_{15}H_{25}OH$ (molecular weight 220.53), combines with lactic acid CH_3CHO HCOOH (molecular weight 89.37) or as lactid $C_3H_4O_2$ (molecular weight taken as 72), to form a monobasic compound of santalol lactate $C_3H_5O_3$, $C_{15}H_{25}$ (molecular weight 291.90).

The theoretical percentage of the lactic radical in santalol lactate therefore is 30.28.

The theoretical percentage of santalol in santalol lactate therefore is 69.74.

The findings of a series of 14 analyses show that the product made by my process closely approximates these figures.

The lactic acid ester of santalol has the following characteristics:

It is reddish brown in color, possesses a sp. gr. of from 1.050 to 1.065, is neutral in reaction, but with a slightly bitter and acidulous taste (possibly due to slight impurity). It is soluble in alcohol, ether, chloroform, acetone, carbon bisulphide, and carbon tetrachloride, but insoluble in water. It has a pleasing but peculiar odor, differing entirely from either of its constituents and slightly recalling that of the terpenes distilled from the *Apium petroselnium* or com-

mon parsley. On heating with alcoholic solutions of KOH or NaOH, it is saponified with liberation of santalol, but is not affected by weak mineral or organic acids. Its boiling point is between 250° and 260° C. at 60 M.M.

I do not pretend to have obtained an absolutely pure santalol lactate, but the commercial process described is practical and the product all that is required for medicinal use in place of sandalwood oil.

HOTEL BREVOORT, May 5, 1911.

RAPID DETERMINATION OF SULPHURIC ACID WITH THE POROUS CLAY CRUCIBLE.

By FREDERICK KLEIN, PH.D.

Every chemist in general will agree that up to the present our methods of gravimetric, and volumetric analysis are apt to have some phase where the accuracy is in doubt, where the reaction is not fully, or in some cases purely hypothetical, and therefore not abso-

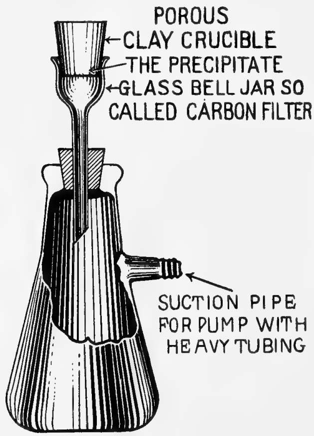

FIG I

lutely correct; we therefore go through journals and chemical literature to find our way out of a labyrinth of reactions which take place by a simple precipitation of two bodies chemically acted upon according to the laws which govern these reactions, visible and ob-

scure, to all our scientific endeavors, methods, instruments, ability and chemically reasoning.

One of the methods which is of the greatest importance and in practical use all over the chemical world is the sulphur determination by barium salts, the considerable time and ability spent to perfect this one method alone would fully prove the correctness of the statement above. In one of the latest Chemical News, the prime and most distinguished German chemical paper *Chem. Ztg.*, No. 135,

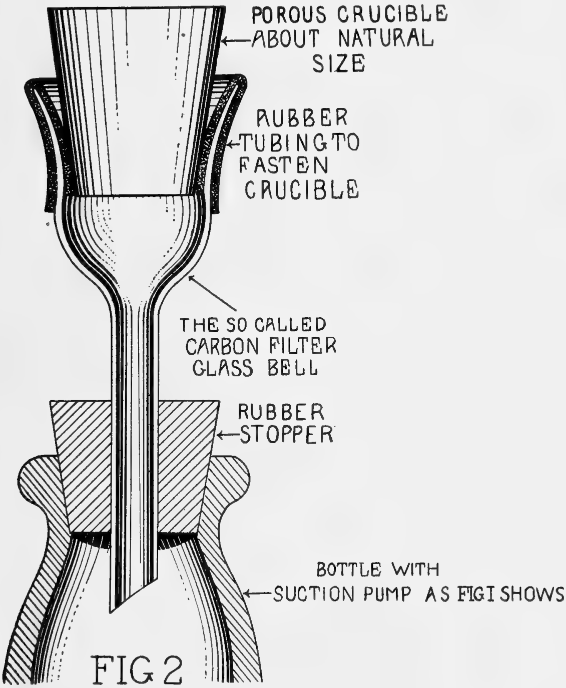

FIG 2

of November 12, on page 1201, we read an article: again stating that the problem of the absolute precipitation of the sulphuric acid with barium salts is still problematic and requires considerable skill and comparatively an absurd length of time to obtain concordant and satisfactory results.

I therefore with pleasure can state, that through the aid of technical progress we have succeeded and obtained a most charming chemical device in the form of a porous clay crucible manufactured by a firm in one of the New England States, and therefore an American production of the highest esteem, and importance to the chemist,

because it fully eliminates the filter paper process, which is one of the most objectionable features in most of the chemical procedures and analytical work of all kind, every chemist will welcome this porous crucible because we all know the difficulty in burning filters, in regard to the ashes and at last, but not least, the reducing action of the carbon of the filter which is highly objectionable, especially in the sulphur determination. These and many other objections which are daily observed in regard to these methods have led me to devise

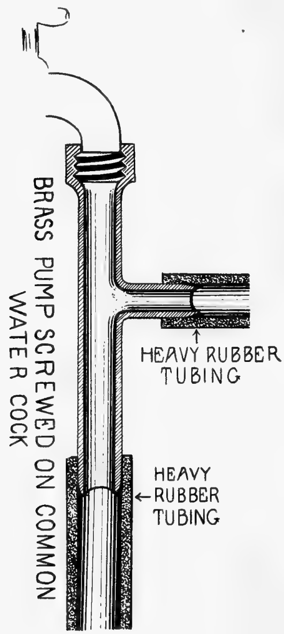

FIG 3

a new porous crucible which enables the chemist to make a dozen or even more sulphur determinations in comparatively the same length of time spent to make a single filter determination considering all points of importance in regard to boiling and addition of barium salts, etc.

Taking the advice of "Hintz" and "Weber" in their extensive study of this especial method, if we operate under the same caution and condition, there arises one and the same inaccuracy which can be tolerated in this method and by the other methods and greatly increase the accuracy after all.

I therefore describe this most simple and rapid determination of sulphuric acid, taking normal sulphuric acid as a standard with 49.05 Gm. of H_2SO_4 to the litre: 10 c.c. of $N/_1$—H_2SO_4 are transformed from a burette or pipette to a beaker of 300 or 400 c.c., the acid is then diluted with three or four times or more by volume of distilled water and boiled for a few minutes; to this solution is added a few c.c. of conc. HCl or HNO_3, stirred, and while boiling add the boiling or hot solution of barium chloride or nitrate 10 or 15 c.c. (10 per cent. solution); stir and mix, and keep mixed solution boiling for a further few minutes; then transfer to a warm place or water bath if convenient to have for settling of the macrocrystalline ppt. While the ppt. settles in water bath the porous crucible is heated and weighed which can be done very easily. I generally weigh the crucible under the same condition without the use of an exsiccator and was able to obtain very satisfactory results.

The weighed crucible is then attached to a water pump of any kind with the so-called carbon filter with rubber stopper, and a moderate stream of water will filter the hot barium sulphate ppt. absolutely clear through the porous clay crucible, leaving ppt. nearly white, and after washing with hot water, or better, slightly acidulated water to free the ppt. from barium chloride or nitrate which can be tested for such with silver nitrate or diphenylamin solution, in the filtrate. The porous crucible with ppt. is then carefully heated with a Bunsen burner and after moisture has been driven off the crucible can then be strongly heated and weighed to constancy.

I have worked out a table based on the principle of normal sulphuric acid 49.05 Gm. of H_2SO_4 to 1000 c.c. Aq. Dest. figuring the acid from barium sulphate from 9 c.c. to 11 c.c. This will enable the chemist to know exactly the strength of acid to dilute or to make stronger if necessary. Ten c.c., which averages to about 0.4905 Gm. H_2SO_4, is about or approximately the sufficient amount of any sulphate to be analyzed, with exception of sulphate ores to more conveniency in some cases to 1 Gm. and more.

This table can also be used for any sulphur analysis considering that the $BaSO_4$ as noted in the table corresponds to the product analyzed.

The crucible as such can be used for the analysis of different colloidal and semicolloidal ppts. with the same accuracy and less time. I have tried the crucible for different analyses and found it to be satisfactory.

NORMAL SULPHURIC ACID.

Factor 0.137 = for sulphur.

Interpolation table between 9 c.c. and 11 c.c.

$BaSO_4 = 233.5$ $H_2SO_4 = 49.05 = \frac{98.1}{2}$

cbcm of $n/_1 H_2SO_4$ contains			cbcm of $n/_1 H_2SO_4$ contains			H_2SO_4 in 1000 c.c.
9.0 c.c.	1.05075	$BaSO_4$	9.0 c.c.	0.44145	H_2SO_4	44.1450
9.1 “	1.062425	“	9.1 “	0.446355	“	44.6355
9.2 “	1.07410	“	9.2 “	0.451260	“	45.1260
9.3 “	1.085775	“	9.3 “	0.456165	“	45.6165
9.4 “	1.09745	“	9.4 “	0.461070	“	46.1070
9.5 “	1.109125	“	9.5 “	0.465975	“	46.5975
9.6 “	1.12080	“	9.6 “	0.47088	”	47.0880
9.7 “	1.132475	“	9.7 “	0.475785	“	47.5785
9.8 “	1.14415	“	9.8 “	0.480690	“	48.0690
9.9 “	1.155825	“	9.9 “	0.485595	“	48.5595
10.0 “	1.16749	“	10.0 “	0.49050	”	49.0500
10.1 “	1.179175	“	10.1 “	0.495405	“	49.5405
10.2 “	1.19085	“	10.2 “	0.50031	“	50.0310
10.3 “	1.2025	“	10.3 “	0.505215	“	50.5215
10.4 “	1.2142	“	10.4 “	0.51012	“	51.0120
10.5 “	1.22587	“	10.5 “	0.515025	“	51.5025
10.6 “	1.23755	“	10.6 “	0.519930	“	51.9930
10.7 “	1.24922	“	10.7 “	0.524835	“	52.4835
10.8 “	1.26090	“	10.8 “	0.529740	“	52.9740
10.9 “	1.27257	“	10.9 “	0.534645	“	53.4645
11.0 “	1.28428	“	11.0 “	0.539550	“	53.9550

$BaSO_4 \times 0.137 =$ Sulphur.

$BaSO_4 \times 0.34286 =$ Factor = Sulphur trioxide.

$BaSO_4 \times 0.420 =$ Factor = Sulphuric Acid.

To multiply factor with Barium Sulphate gives either S, SO_3 or H_2SO_4.

The following is an addition to the interpolation table:

1.	2.	3.	4.
9.0 to 9.1	9.9 to 10.0	10.0 to 10.1	10.1 to 10.2
0.051917	1.156992	1.168667	1.180342
0.053084	1.158159	1.169834	1.1815092
0.054251	1.159326	1.171001	1 182676
0.055418	1.169493	1.172168	1.183843
0.056585	1.161660	1.173335	1.185010
0.057752	1.162827	1.17450	1.186177
0.058919	1.163994	1.175669	1.187344
0.060086	1.165161	1.176836	1.188511
0.061253	1.166328	1.178003	1.189678
0.06242	1.167495	1.17917	1.190845

Example: it has been found upon using 10 c.c. of H_2SO_4 that *1.173335* $BaSO_4$ by weight, was obtained. Upon consulting table 3 this denotes that the solution of H_2SO_4 is 5/100 or 0.05 in 10 c.c. too strong.

THE ADRENALIN PATENTS VALID.

THE UNITED STATES CIRCUIT COURT SO DECIDES.

When the physiological and therapeutic value of the suprarenal gland had become fully established, several prominent chemists, believing its valuable properties to be due to an active principle, studied strenuously to isolate it. Two at least came very near success. It remained for Dr. Jokichi Takamine, however, to achieve the sought-for result, and he secured basic patents covering the substance, its salts and solutions, simultaneously publishing his methods. Other investigators afterward claimed to have isolated the active principle, and there appeared on the market, in addition to Adrenalin, similar preparations under other names.

It became a much-mooted question whether Dr. Takamine was entitled to priority, and whether the patents were valid. Parke, Davis & Co. purchased the Doctor's rights in consideration of a royalty, under agreement that payment of the royalty should cease if the patents were invalidated. To determine the question of the validity of the patents two suits were brought against the H. K. Mulford Company in 1905, involving these questions: First, Are Adrin and Adrin Solutions infringements of the patents covering Adrenalin and Adrenalin Solution, respectively? Second, If so, are these patents valid? Upward of five years was consumed in taking expert testimony respecting the history of the discovery, etc., and the hearing was not had until February 3, 1911, when the matter was submitted on argument, the records and briefs covering over a thousand closely printed pages.

Saturday, April 29th, Judge Hand, of the United States Circuit Court for the Southern District of New York, handed down an elaborate opinion answering both questions affirmatively. The effect of this opinion is that other substances similar to Adrenalin, and called by other names, are infringements of the Takamine patents.

Concluding, Judge Hand says:

"Whatever confusion the intricacy of the subject matter causes, one fact stands out which no one ought fairly to forget: Before Takamine's discovery the best experts were trying to get a practicable form of the active principle. The uses of the gland were so great that it became a part of the usual therapy in the best form which was accessible. As soon as Takamine put out his discovery, other forms practically disappeared; by that I do not mean abso-

lutely, but that the enormous proportion of use now is of Takamine's products. There has been no successful dispute as to that; hardly, indeed, any dispute at all. What use remains is, so far as the evidence shows, of the old dried glands, which every one concedes to have been dangerous, at least for intravenous use. All this ought to count greatly for the validity of the patent, and Takamine has a great start, so to speak, from such facts. . . . He has been author of a valuable invention, and has succeeded where the most expert have failed."

The litigation has been conducted in the most friendly spirit between the two great houses concerned. Parke, Davis & Co. had nothing to lose, since, had the patents been declared invalid, they would not longer have been handicapped by the payment of royalty, but could have marketed upon equal terms with competition. As it is, under their arrangement with Takamine, they are entitled to the exclusive right to manufacture and sell the active principle of the suprarenal gland, its salts and solutions, during the life of the patents, after which the Doctor's processes, as well as his products, will become *publici juris.*

CORRESPONDENCE.

AMERICAN PHARMACEUTICAL ASSOCIATION.

Editor American Journal of Pharmacy:

Enclosed please find an announcement of the preliminary arrangements for the approaching meeting of the A. Ph. A.

Kindly use as much of it as you can give space for, and I will supplement this notice with more specific details as they are finally determined upon.

Our members are enthusiastic and promise great things in the way of entertainment, and we are assured that the meeting will be a most successful one.

Yours sincerely,

C. Herbert Packard.

THE AMERICAN PHARMACEUTICAL ASSOCIATION AT BOSTON, AUGUST 14 TO 18, 1911.

The meeting of the American Pharmaceutical Association at Boston in August promises to be one of the most successful meetings in the history of this honorable scientific organization.

Boston is an ideal city for a summer convention and the doors of her warm-hearted hospitality are being set wide-open to welcome with the most diligent service of heart and hand, her friends of the East, the West, the Southland and the Northland, whose smiling faces and cheery welcomes have so often made the Boston pharmacists feel at home with them.

While Boston's welcome to the association will be a warm one, yet one need not think it attributable to the temperature, for Boston is never sultry; the breezes from Massachusetts Bay, which are nearly always in evidence, making the city cool when places inland are sweltering in heat.

Beyond the natural interest which the scientific pharmacist will have in the interesting and instructive meetings at which will be gathered the leaders of pharmaceutical thought of this and foreign countries, the other many and varied attractions of St. Botolph's town appeal to every one and draw them irresistibly to that city, for without the inspiring memories which throng around it, there would be no American pharmacy. Its streets were trod by Warren, by Adams, by Revere and by Hancock, and the first American blood shed for our independence flowed in its streets. Around and about the city are Lexington and Concord, Bunker Hill and Dorchester Heights; Plymouth with its historic "Rock," where the Pilgrims established the first American Commonwealth, "In the Name of God, Amen!"; Cambridge with its memories; John Harvard and his college, with its treasures of surpassing interest in its Germanic Museum and other interesting collections, its reminiscences of Longfellow and of Lowell; Salem, the Witch City and its House of Seven Gables of Hawthorne; Gloucester with its "Reef of Norman's Woe"; and Marblehead, through whose streets "Old Floyd Ireson was carried in a cart"; Amesbury and Haverhill with their memories of "The Quaker Poet," Whittier.

Around Boston is an inexhaustible mine of history and memories among which the visitors to that city may delve for weeks to their interest and profit.

The Committee on Entertainment, under the energetic lead of Mr. C. Herbert Packard, the Local Secretary, is working diligently to assure to every member in attendance a most pleasurable occasion, with the avowed purpose that all will ever remember it as an event in their lives. The co-operation of the Chamber of Commerce, an organization of 3000 leading business men of Greater Boston, has

been pledged, and its President, Mr. George S. Smith, will probably welcome the association to the city; Governor Foss and Mayor Fitzgerald have both earnestly assured the committee of their desire to extend to the members a true Boston welcome.

The headquarters of the association will be at the Hotel Vendome, one of the noted hotels of this continent, whose walls have sheltered royalties in their visits to Boston. This hotel is located on the famous Commonwealth Avenue, one of the finest residential avenues in the country; within a stone's throw of this hotel is the noble Copley Square, which is undeniably one of the finest public squares of the world, vying for pre-eminence with the Place de la Concorde in Paris.

The meetings of the Association will be so arranged as to give abundant time for sight-seeing, and the ladies who accompany the members will be taken into the assiduous care of the Ladies' Entertainment Committee, of which Mrs. Adelaide Godding, the wife of the President-elect of the association, is chairman; and it is therefore certain that not an idle or a tedious moment will be allowed to intrude its attention upon any of the fair visitors during their visit to the Hub.

The Committee on Entertainment say that the old adage, "See Naples and die," has been recently revised and now reads, "See Boston and live; enriched for all time with the memory of its treasures, and of its hearty New England welcome."

COME TO BOSTON!!!

BOOK REVIEWS.

ORGANIC CHEMISTRY FOR THE LABORATORY. By W. A. Noyes, Ph.D., Professor of Chemistry in the University of Illinois. Second Edition, Revised and Enlarged. Easton, Pa., The Chemical Publishing Company. 1911.

Professor Noyes has well stated in his preface to the first edition of his "Laboratory Manual" that "the science of organic chemistry rests, for its experimental foundation, on the preparation, usually by synthetic means, of pure compounds. Without a knowledge, based on personal experience in the laboratory, of the relations involved and the methods which may be used in such preparations, no satisfactory knowledge of the science can be acquired."

The book has been well conceived and well developed, and it will not only be found useful to the student, but also of special value to the advanced worker, as it is full of suggestions. The most important laboratory processes which have been worked out in the development of organic chemistry are considered. The directions are full and accurate, and the theoretical explanations of the processes are clear and concise.

In addition to much valuable information, as found in the chapters on the general operations, the analysis of carbon compounds, and the qualitative examination of such substances, the methods for the preparation of 131 separate compounds are given. These include hydrocarbons; alcohols and phenols; ethers; aldehydes, ketones and their derivatives; acids; derivatives of acids; hydroxy and ketonic acids; carbohydrates; halogen compounds; nitro compounds; amines; diazo, hydrazo, nitroso and other nitrogen compounds; and sulphur compounds.

While this book has been prepared especially for the organic chemist, it will be found of very great service to the manufacturing pharmacist. Indeed, the pharmacist, who spends some of his time in the laboratory will be stimulated in his work, and will be well repaid if he adds to his desk library this new edition of Noyes's "Organic Chemistry for the Laboratory."

The Fats. By J. B. Leathes, M.A., M.B., F.R.C.S., Professor of Pathological Chemistry in the University of Toronto. Longmans, Green & Co., London, New York, Bombay and Calcutta. 1910. 4s. net.

This is the eleventh of the series of monographs on "Biochemistry" edited by Drs. Plimmer and Hopkins. These are exceedingly valuable books. Each monograph has been prepared by a specialist, and contains a complete bibliography. The contents of the present volume include: (1) the fatty acids, glycerol and the glycerides, other alcohols and their fatty acid esters, phospholipines, galactolipines and lipines; (2) the extraction of fat, and the estimation of fat in animal tissues; (3) physical properties of fats, general chemical methods used in analysis of fats, separation, identification and constituents of fats:—fatty acids, alcohols and phospholipines; (4) the physiology of fats: biochemical synthesis of fats and higher fatty acids, physiological oxidation of fats and the rôle of fats in vital phenomena.

The book is especially intended for the use of physiologists and biochemists. It contains, however, much information that the dispensing pharmacist could use to advantage. In the making of ointments, the preparation of emulsions and the manufacture of substances containing fatty constituents, he would obtain hints that would enable him better to co-operate with the physician and discern the objects he has in mind and why certain classes of fats apparently give more satisfactory results than others in given conditions.

A Systematic Handbook of Volumetric Analysis or the quantitative determination of chemical substances by measure, applied to liquids, solids, and gases. By Francis Sutton, F.I.C., F.C.S., Public Analyst for the County of Norfolk, etc. Tenth Edition, revised throughout with numerous additions by W. Lincolne Sutton, F.I.C., Public Analyst for the County of Suffolk, Norwich, Ipswich, etc., and Alfred E. Johnson, B.Sc., Lond. Philadelphia: P. Blakiston's Son & Co., 1911. $5.50 net.

It is now nearly fifty years since the first edition of Sutton's "Volumetric Analysis" was published. This year the elder Sutton celebrates his jubilee as a Fellow of the Chemical Society, and well may the members rejoice with him in recognition of his achievements and the useful work which he has done in pure and applied chemistry. Not only has Sutton's "Volumetric Analysis" been used by the pharmacist, manufacturing chemist, pathological chemist, etc., but it has also been adapted to the requirements in pure chemical research. And this may be taken to explain the secret of the success of the work. The author, having before him an ideal and being fully cognizant of the importance of research in advancing knowledge, has nevertheless utilized the results of research workers in the various fields of applied chemistry.

It is indeed an inspiration to read the author's preface in this the tenth edition and find his enthusiasm unabated and his optimism as great apparently as in 1863, when the first edition came from the press. He says: "An exceptionally long interval of seven years has elapsed since the publication of the last edition of this work, whilst it has been out of print for nearly eighteen months, a fact which is without precedent in its history. The interval has not left me a younger man, and I must confess that as the time for a new edition approached I have found myself, at the age of four-score years, less equal to the task. So large and so constant is the work now being

done in the domain of volumetric analysis, that the need of reconsideration of old methods and of selection from amongst the newer methods becomes more imperative with each succeeding edition of a book of this character. The present, moreover, being the tenth edition, I was particularly anxious that it should be distinguished by the most thorough and critical revision yet attempted, and, in the result, by the greatest possible consonance with modern practice. To this end, I placed its preparation entirely in the hands of my son and partner, W. Lincolne Sutton, who had accumulated a large amount of material in anticipation, and of Mr. Alfred E. Johnson, . . . who had rendered me valuable and acknowledged assistance in the course of preparing the ninth edition. I feel that I cannot pay too generous a tribute to the devotion of both editors to the task they undertook. . . . I must admit that the result has rather damaged my conceit as an author, for it is obvious that many possible improvements will reveal themselves under a meticulate examination in a book which has grown, as this has, by a process of accretion tempered by pruning and extended through nine editions over a period of forty years. I am sensible that much remains to be done, but am sanguine enough to be looking forward already to the next and jubilee edition, when the book will have attained its fiftieth year."

The editors have done their work exceedingly well. Much of the matter in the ninth edition has been entirely rewritten. It has been critically revised throughout, obsolete matter has been eliminated, but the general scope and original features of "Sutton" are retained. For pharmacists who do analytical work this latest edition of Sutton's "Volumetric Analysis" will be indeed welcome.

Materia Medica Step by Step. By Arthur W. Nunn, F.C.S. London: J. & A. Churchill; also P. Blakiston's Son & Co., Philadelphia. 1911. $1.40 net.

This is one of those books that a reviewer does not like to criticise. It is always unpleasant in commenting on a book "to damn with faint praise." But the impression on glancing at this book is not favorable. One or two illustrations will suffice to show this: The author says: "Inulin is a kind of starch. . . . It can be distinguished from potato and other starches by the fact that when hydrolised it yields *levulose,* whereas the other starches when treated in the same way yield glucose."

Again, he says: "Cellulose is another kind of starch. It . . . may be distinguished from starch by its resisting the action of potassium chlorate and nitric acid."

But why call further attention to examples such as these? For him who uses the book it means "step by step" to failure.

NEW AND NON-OFFICIAL REMEDIES 1911. Containing descriptions of the articles which have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association, prior to January 1, 1911. Chicago: Press of the American Medical Association, 535 Dearborn Avenue. 1911.

As stated by the Secretary of the Council in the preface, "The acceptance of the articles included in the book has been based in part on evidence supplied by the manufacturer or his agent, and in part on investigation made by or under the direction of the Council." Furthermore, we read: "The Council desires physicians to understand that the acceptance of an article does not necessarily mean a recommendation, but that so far as known it complies with the rules adopted by the Council."

There are some ten official rules of the Council on Pharmacy and Chemistry of the A. M. A. The nature of them is probably best understood in their object. They have been adopted "with the object of protecting the medical profession and the public against fraud, undesirable secrecy, and objectionable advertising in connection with proprietary medicinal articles." It is not too much to say that the Council on Pharmacy and Chemistry of the A. M. A. has done for the cause of medicine what the Bureau of Chemistry of the U. S. Department of Agriculture has accomplished in the interest of pure foods. The Council has the support of the medical profession in the same sense that the Bureau of Chemistry has the support of the members of that profession. The work of the Council is a most difficult and delicate one and yet a very necessary and fundamental one when we consider the almost bewildering number of compounds, many of which have absolutely no claim to merit, that are foisted on the medical profession each year. Some such course as this seems imperative if the profession in general would free itself from the stigma of quackery. To the younger practitioners the work of the Council should be especially helpful. Retail pharmacists generally must also appreciate the value of it and should procure copies of "New and Non-official Remedies, 1911," which

may be obtained at a merely nominal charge by addressing the Secretary, Prof. W. A. Puckner, 535 Dearborn Avenue, Chicago, Ill.

DIGEST OF COMMENTS on the Pharmacopœia of the United States of America and the National Formulary for the Calendar Year ending December 31, 1908. By Murray Galt Motter and Martin I. Wilbert. Washington: Government Printing Office. 1911.

Only the student who has experienced the grind of looking up the literature in connection with his investigations can appreciate to the fullest extent the value of the "Digest of Comments." Up to within recent years, since the appearance of the first number of "Digest of Comments," the reviewer spent much time noting articles and conserving clippings of subjects he wished to keep informed concerning. This is all unnecessary now with articles pertaining to the Pharmacopœia and National Formulary. It is very simple to take down the volumes of the "Digest of Comments" and quickly turn to the subject of the article one is working upon. There will be found, with abstract, references to all of the published papers on the subject during any one year. Not only this, but the foreign Pharmacopœias are reviewed and valuable tables are given showing the relationship of the preparations in the different pharmacopœias.

OBITUARY.

CALEB R. KEENEY.

In the death of Caleb R. Keeney, the retail drug trade has lost one of the best types of the profession. Mr. Keeney was born in Carlise, educated there, and apprenticed to the 1st Henry Blair, who had his store where the 3d Henry C. Blair is now at Eighth and Walnut Streets, Philadelphia.

Mr. Keeney at the termination of his apprenticeship commenced business for himself at Sixteenth and Arch Streets, and continued there until the day of his death; his son having been associated with him for thirty-five years and succeeds to the business.

There are not many drug pharmacists in Philadelphia to-day who have remained so close to the calling. He was what Prof. Parrish said a druggist was in his neighborhood: An "Oracle" as it were. The Professor in speaking of the druggist said that he

was supposed to know everybody of any account in his section, and that the public found this generally to be true. I am sure that even to-day if one wishes to ascertain the residence of a person his first inquiry would be at the nearest drug store. Mr. Keeney saw many changes in his immediate section; the old families vanished and new people came into the neighborhood. Other stores at times came into existence near him, but nothing could impair the confidence reposed in him and his store by his neighbors and the medical profession. There is not a store in Philadelphia to-day where legitimate pharmacy is more in evidence than in the old store of Mr. Keeney. Living for a time near him and frequently dropping in I do not remember seeing a proprietary or many of those other rather inconsistent items that most stores display.

Mr. Keeney graduated from our College in the class of 1846 and was at the time of his death the oldest living graduate. In the same class was the late Thomas S. Wiegand. He was a member of the College and for many years of the American Pharmaceutical Association. Of quiet tastes he won the esteem of all who were brought into contact with him, and it is gratifying to know that the pharmacy will no doubt be carried on in the same lines by his son, who has been with him for 35 years. He died February 1, 1911, in his eighty-sixth year, after a short illness. He leaves a son

E. T. ELLIS.

PHARMACEUTICAL MEETINGS.

MARCH MEEETING.—The sixth of the pharmaceutical meetings was held on March 15, with W. L. Cliffe in the chair. At this meeting, two papers were read, treating of the subject of petrox preparations. The first of these papers was by Mr. Geo. M. Beringer, Ph.M., and George M. Beringer, Jr., P.D. This paper is the result of a rather extensive series of experiments which have been carried out by the authors in order to recommend the most satisfactory formulæ for the petrox preparations of the National Formulary. A large number of preparations were shown and the entire paper is published in the May issue of this JOURNAL.

The paper by Mr. Raubenheimer is also published in this issue and was in the nature of a supplementary work to that of the pre-

ceding paper, in fact the results obtained by Mr. Beringer and his son were confirmed by Mr. Raubenheimer (see p. 223).

April Meeting.—The seventh of the pharmaceutical meetings was held on Tuesday, April 18th, with Dr. C. A. Weidemann in the chair. Professor C. B. Lowe gave an interesting talk upon "Pharmaceutical Economics." He exhibited a number of pieces of apparatus illustrating the making of emulsions, tablet triturates, filling of capsules, gelatin coating of pills, etc. He also called attention to a method which is sometimes useful in preventing the directions upon prescription bottles from becoming indistinguishable by reason of the liquid flowing on the outside when used by the patient. The directions are pasted next to the bottle and can readily be seen looking through the bottle from the opposite side. This is particularly useful in preserving the number of the prescription and the copy of the same. The number being helpful to the pharmacist and the copy useful to the physician.

Professor Kraemer exhibited the collection of drugs of the Japanese Pharmacopœia which he had received from one of the Honorary members of the College, Dr. W. N. Nagai of the University of Tokyo. The specimens were in large glass stoppered bottles, made a splendid exhibit and included the following: Amylum Erythroni (Katakuri), obtained from *Erythronium dens-canis* L.; Amylum Puerariæ (Kazu) obtained from *Pueraria Thunbergiana* Benth.; Radix Coptidis (Orea) Tamba, obtained from *Coptis anemonæfolia* S .et Z.; Radix Coptidis (Oren) Kaga, obtained from *Coptis Art;* Radix Gentianæ Scabræ (Riutan), obtained from *Gentiana scabra* Bge. *var. Buergeri* Maxim.; Radix Phytolaccæ (Shoriku) obtained from *Phytolacca acinosa* Roxb. *var. esculenta* Maxim.; Semen Pruni Armeniacæ (Kiyonim) obtained from *Prunus Armeniaca* L.; Folia Pruni Macrophyllæ (Bakuchi yo) obtained from *Prunus macrophylla* S. et Z.; and Radix Taraxaci cum Herba (Hokoye) obtained from *Taraxacum officinale* Wigg. *var glaucescens* Kock.

May Meeting.—The last of the series of meetings for 1910 and 1911 was held on May 16th, Mr. Henry C. Blair presiding. The meeting was given over to the members of the graduating class for the presentation and discussion of their theses. The following gave abstracts of the same: Morris Haimowitz, Samuel Millrood, Julius G. Rappaport, W. W. Rose and Frank X. Hedges. Abstracts of some of these theses will be published in later issues of this Journal.

Notes and News.

Prof. Oscar Oldberg received the honorary degree of Doctor of Laws at the commencement exercises of Northwestern University on June 14, 1911.

Samuel W. Fairchild, former president of the College of Pharmacy of the City of New York was awarded the honorary degree of Master of Science at the commencement exercises of Columbia University on June 27, 1911.

Prof. J. W. Sturmer of Purdue University was awarded the degree of Doctor in Pharmacy at the commencement exercises of Buffalo College of Pharmacy on June 1st, 1911.

Dr. Julian W. Baird, Dean of the Massachusetts College of Pharmacy, died on June 26, 1911. Funeral services were held at the college building on June 28, 1911.

Prof. Harry Vin Arny, Dean of the Cleveland School of Pharmacy, has been appointed to the chair of Chemistry in the College of Pharmacy of the City of New York, succeeding Prof. Virgil Coblentz, who resigned to take charge of the analytical department of E. R. Squibb & Sons.

Dr. E. F. Kelley, superintendent of the laboratories of Messrs. Sharp and Dohme, has become director of the Pharmaceutical Laboratory of the School of Pharmacy, University of Maryland.

Prof. John Attfield, the eminent English chemist and one of the leading authorities in pharmaceutical chemistry, died on March 20, 1911. A very complete biographical sketch of Professor Attfield, written by F. A. Upsher Smith, was published in the March issue of this Journal for 1906. An excellent portrait of Professor Attfield also accompanies this article.

Professor Attfield was "a man of many interests, and whatever his hand found him to do he did that with all his might. And he did many things. He was one of the founders of the British Pharmaceutical Conference, for many years Editor of its Transactions, for 17 years its senior Secretary, and on two occasions its President. His connection with the British Pharmacopœia began in 1882 and ceased on the publication of the 1898 edition and the issue in 1900 of the Indian and Colonial Addendum."

His body was cremated at Golder's Green and in addition to the members of the family who attended the services, were a number of representatives of societies with which Professor Attfield had a prominent connection.

From photograph made by Underwood and Underwood, New York

HARVEY WASHINGTON WILEY

THE AMERICAN
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AUGUST, 1911

THE ESTIMATION OF MINUTE QUANTITIES OF NITROGLYCERIN.*

By Wilbur L. Scoville.

From a medicinal point of view the estimation of nitroglycerin offers peculiar difficulties. This drug acts powerfully on the human system and is given in doses from 1/1000 to 1/20 grain. The most common form of administration is in tablets, and a method of determining the strength of these with accuracy is much to be desired.

For pharmaceutical purposes nitroglycerin is obtained in 10 per cent. alcoholic solution, which is practically a saturated solution, or in about 20 per cent. admixture with absorbent powders, as sugar of milk, chalk, talcum, etc., to which a little bicarbonate of sodium or carbonate of magnesium has been added for safety in shipping. There is evidence that both the solution and the powder-mixture deteriorate slowly. In cold weather a portion of the nitroglycerin will separate from the alcoholic solution, leaving the liquid weak unless the precaution is taken to warm and redissolve. Furthermore as L. H. Bernegua has pointed out [1] there is a loss in the process of manufacturing tablets of nitroglycerin, and the accuracy of the tablets is not therefore a question merely of mathematics and careful workmanship.

For the estimation of nitroglycerin in pharmaceutical preparations, two methods are in general use,—the nitrometer method, and titration after saponification with standard alcoholic potash. Of these the nitrometer method is undoubtedly the more accurate, and

* Read at the Indianapolis meeting of the American Chemical Society, July, 1911.

[1] *Amer. Jour. Phar.* 1907, page 555.

is probably the more used. For standardizing the stronger alcoholic solutions and the powder-mixtures (precautions being taken to exclude the carbonates present in the latter) it may give good results in skilled hands.

But the nitrometer requires experience in its use, and particularly for this substance. Newfield and Marx in an article on the use of the nitrometer[2] with special reference to the examination of nitrocellulose, a kindred body of nitroglycerin,—state that the sulphuric acid used must not be below 94.8% strength, the time of agitation not less than 3 minutes, and that the presence of other organic bodies may seriously affect the results. They say that "a great number of details, some of them apparently trivial, affect the results to a considerable extent." If we add to these the difficulty of weighing accurately and transferring completely to a nitrometer, so viscid a substance as nitroglycerin, without unduly diluting it in the transferring, it is not to be wondered at that one unacquainted with all of these necessary details should obtain results varying from 82% to 108% in half a dozen assays on the same sample, and become discouraged thereby, although accustomed to the nitrometer in the assay of ethyl nitrite. Hence the statement often made that "experience is necessary" in the use of the nitrometer for nitroglycerin assays, cannot be too strongly emphasized.

Furthermore for the estimation in tablets there are additional difficulties.

The method of estimating nitroglycerin by saponification with alcoholic potassium hydroxide has been proposed by several writers.

Mr. Hay states[3] that the decomposition of nitroglycerin by alcoholic potash is of a complex nature, the products being potassium acetate, oxalate and formate, free ammonia, etc. Nevertheless he offers an equation wherein 5 molecules of potassium hydroxide act upon 1 molecule of nitroglycerin to give the above, and proposes that equation as the basis of assay by titration with standard alcoholic potash and standard acid.

In 1895 Dr. Charles Rice recommended[4] the estimation of nitroglycerin by saponification with standard potassium hydroxide and standard acid, on the basis that the reaction products are simply potassium nitrate and glycerin. The high position and reputation

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[2] *Jour. Amer. Chem. Soc.*, 1906, page 877.

[3] *Jour. Chem, Soc.*, 1885, page 742.

[4] *Amer. Drug. & Pharm. Rec.* July 10, 1895, page 6.

of Dr. Rice gave this process an immediate standing, and it has since been endorsed by several writers, notwithstanding that it was pointed out as early as 1868 by Tilberg[5] a Swedish chemist that the reaction between potassium hydroxide and nitroglycerin is not a simple but a very complex one, and results in nitrite, cyanide, oxalate and formate of potassium and free ammonia, and that in 1885 Mr. Hay reiterated this fact. The endorsements of this process, as well as Dr. Rice's own experiments appear to be based on the fact that *expected* results are frequently obtained by it, but without any proof that *expected* results were *correct* results.

In 1910, Berl & Delpy[6] stated that when cold alcoholic solution of potassium hydroxide is mixed with nitroglycerin, and the temperature kept under 25° C. for some time, the products of reaction are potassium nitrate, nitrite, cyanide, oxalate, mesoxalate and formate, aldehyde, ammonia, glyceryl dinitrate and glyceryl trinitrate—(some of the last remaining undecomposed). They further state that 6 molecules of potassium hydroxide are required to decompose one of nitroglycerin and that the reaction is not complete in the cold.

Here then there is one chemist (Hay) who says that one molecule of nitroglycerin requires 5 molecules of alkali, another (Rice) that 3 molecules of alkali are required, and a third (Berl & Delpy) that 6 molecules are necessary.

And one has only to try the process, varying the conditions of heating, the time of standing, and the temperature, to become convinced that the results are of no value.

Indeed one is surprised to note how much variation in results is induced by slight variations in the process.

In 1905, Binz[7] a Swedish chemist proposed to estimate nitroglycerin by saponifying it with alcoholic potash, reducing the nitrate, cyanide, etc., so formed to ammonia by treating the liquid with nascent hydrogen (formed by zinc and sulphuric acid added to the liquid) then estimating the ammonia, after distillation. In this process the nitrogen is first converted entirely into ammonia, and the latter estimated. This appears to be scientifically sound, and if conditions can be made to ensure complete reaction without loss of nitrogen in any form, it may give accurate results. The writer has not tried

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[5] Proc. A.Ph.A., 1869, page 242.

[6] *Ber.* 43 1421 thro. Chem. Abst., 1910—2488.

[7] Year Book Pharm., 1906, page 53.

it. It suggests the Kjeldahl method of estimating nitrogen,—which the writer has tried on nitroglycerin with good results.

For pharmaceutical purposes the need applies particularly to an estimation of minute quantities, as in 1/100 grain tablets, etc.

The writer first attempted to use "nitron" for this purpose but the insolubility of nitroglycerin in water makes this impracticable.

The use of phenol disulphonic acid, as in water analysis for the estimation of nitrates, then suggested itself. On trial this worked well, and appeared to give excellent results. It then remained to ascertain whether such results were correct.

Since this reagent must be applied to a dry residue, the first question relates to the volatility of nitroglycerin, some writers having asserted that it is slightly volatile.

A (supposedly) 10% alcoholic solution was evaporated under three conditions, two samples of 10 c.c. each being used for each test.

No. 1 the alcohol was driven off on a steam bath, the residue being removed from the bath before the last traces of alcohol had disappeared, then dried in a vacuum desiccator.

No. 2 was subjected to a blast of warm air until the alcohol had been dissipated, then dried in a vacuum desiccator.

No. 3 was placed in a vacuum desiccator and the vacuum maintained during 60 hours.

The residues weighed:

No. 1	A = 1.030	(b) = 1.029	Gm.
No. 2	A = 1.0135	(b) = 1.0115	Gm.
No. 3	A = 1.027	(b) = 1.032	Gm.

On subjecting some of these residues to a moderate heat, as on top of a steam-bath, above and removed from a steam-bath, on warm sand, etc., they all lost weight with varying rapidity, while residues which were maintained in a vacuum in the desiccator and weighed daily, lost only 1.5 and 1.6 milligrams in 6 days. It was further learned that when in evaporating the alcohol by aid of a very moderate heat—(40° to 50° C.) if the residue was left in the heat after the alcohol had disappeared, the results were lower and were uneven. It appears therefore that *nitroglycerin is not volatilized even in a vacuum in ordinary temperature but that dry nitroglycerin is slowly decomposed by a very moderate temperature.* This sample of solution had a density of 0.8650 at 25° C. and tested by the Kjeldahl-

Gunning method gave 8.642, 8.717, 8.732 and 8.822 per cent. of glyceryl trinitrate,—average 8.72 per cent. w.v. The evaporation method therefore gives high, though uniform results.

In operating the Kjeldahl-Gunning method there is trouble with frothing unless the alcohol is first driven off completely, a troublesome matter to operate without loss in a Kjeldahl flask. The precaution must also be taken to entirely dissolve the nitroglycerin in the acid before heating, a matter which requires a thorough shaking and a little patience, but avoids subsequent loss by minute explosions.

Tested by the phenoldisulphonic acid method this solution showed 8.3 per cent. w.v., which, considering the minute quantity used for this test, is very satisfactory.

Two other samples of the same order-lot of solution, but taken from different containers, were tested by the evaporation, Dumas, Kjeldahl-Gunning, and the colorimetric methods. The results follow:

Solution No. 2.	Spec. Grav. at 26° C. 0.8390.
Evaporation method	5.91 per cent. and 5.84 per cent. w. v.
Dumas (combustion) method	5.79 per cent. 5.85 and 5.84 per cent. w. v.
Kjeldahl-Gunning	5.82 per cent. w. v.

Solution No. 3.	Spec. Grav. at 25° C. 0.8536.
Evaporation method	8.83 and 8.85 per cent. w. v.
Dumas (combustion) method	8.534 per cent. and 8.545 per cent. w. v.
Kjeldahl-Gunning	8.42 per cent. w. v.

From each of these, dilutions were made to contain 1 gram of nitroglycerin in 100 c.c. of alcohol solution, at 20° C. calculated from the Dumas estimation, and these dilutions were tested by the colorimetric (phenoldisulphonic acid) method. Each of four solutions tested 1 gram in 100 c.c. colorimetrically.

This method therefore gives as accurate results as a colorimetric method may, and for the estimation of minute quantities is greatly to be preferred.

The method of applying the test is essentially the same as is used in water analysis. The standard solution of potassium nitrate was used as standard. This is made by dissolving 0.722 (0.7217) gram of pure fused potassium nitrate in sufficient water to make 1000 c.c. One c.c. of this solution contains 0.0001 gram nitrogen in the form of nitrate and 1.2 c.c. of this solution contains the same amount of nitrogen as 1/100 grain of pure nitroglycerin. Of the alcoholic solutions the equivalent of 0.00065 Gm. (or 1/100 grain) of pure

nitroglycerin (calculated) was measured into a small porcelain evaporating dish, and allowed to evaporate spontaneously. Into another dish was measured 1.2 c.c. of the standard nitrate solution and evaporated at a low temperature. When both were dry 2 c.c. of the phenoldisulphonic acid reagent were added to each, the mixture stirred well with a glass rod and allowed to stand 10 minutes, then diluted with water, rendered slightly alkaline with potassium hydroxide, cooled and diluted to 100 c.c.—or 200 mm. in the comparison tubes. The colors were then compared in a Schreiner colorimeter in the usual way.

If a colorimeter is not at hand, Nessler tubes will give very good satisfaction. In the colorimeter a difference of $^1/_{20}$ or 5 per cent. is easily discerned.

For tablets, five $^1/_{100}$ grain tablets are powdered, 10 c.c. of alcohol added and the mixture shaken frequently during 1 to 2 hours, then filtered.

Two c.c. of the clear filtrate is then evaporated and treated. Other strength tablets are treated similarly, the equivalent of $^1/_{100}$ grain being taken for test. If the tablets are easily friable they are broken up with a glass rod after adding the alcohol.

The test, so far as tablets are concerned was proven by adding a known alcoholic solution of nitroglycerin to varying quantities of sugar of milk, drying without heat then treating with alcohol as above and applying the test. The full amount of nitroglycerin put in was recovered by the test, except in one instance when an excessive amount of sugar of milk was used.

A sample of the U.S.P. Spirit of Nitroglycerin containing 1 per cent. by weight of nitroglycerin was made from solution No. 3.

The specific gravity of this at 25° C. is 0.81378. Ten c.c. of it made a clear mixture with 12 c.c. of water at 15° C., but 13 c.c. at this temperature produced a marked milkiness.

The present U.S.P. tests on this spirit allow so wide a range as to be of little value. The above sample has been kept six months and shows no change in strength.

VARIATIONS IN THE FORMS OF DIGITALIS HAIRS.[1]

By Henry Kraemer.

While considerable attention has been given in a general way to the pharmacognosy of digitalis, these studies have for the most part aimed to differentiate digitalis from other leaf drugs which may have been occasionally substituted for the genuine drug. As a matter of fact the adulteration of this drug or its substitution is very rare indeed. When we consider that digitalis has been used in medicine for some 400 years and see the conflicting statements that are still made regarding the efficiency and deterioration of the drug and its preparations, we may well ask how much progress has been made in the solution of the problems which this drug with its complex constituents presents. It is true that we have methods for the biological standardization of the drug and its preparations but these do not enable us to determine in advance which lot of drug will, in a given instance, be found valuable and which will be of inferior quality. It is not too much to claim that no work on such an important drug as this will be complete until we can determine either by chemical analysis or through pharmacognostical studies the differences between different samples of drug. One thing that is needed, then, owing to the complexity of the chemical constituents, is more or less extended work in conjunction with pharmacological tests having in view a closer differentiation of the physical and microscopical characters of the specimens examined. It is true that we have in the various pharmacopœias such statements as, that the leaves only of the second-year plant shall be used, and at the present time there is a tendency to require that the leaves shall be thoroughly dried and kept in containers with freshly burnt lime. But we find that recent investigations tend to show that the leaves of the second-year plant are relatively but slightly more potent. And again, we know that certain practitioners use only the tincture of the fresh drug. Furthermore, there is a tendency in many quarters in spite of the restrictions in many pharmacopœias that the leaves only of wild plants shall be used, to employ the leaves of cultivated plants, and

[1] Presented at a meeting of the Pennsylvania Pharmaceutical Association, June, 1911.

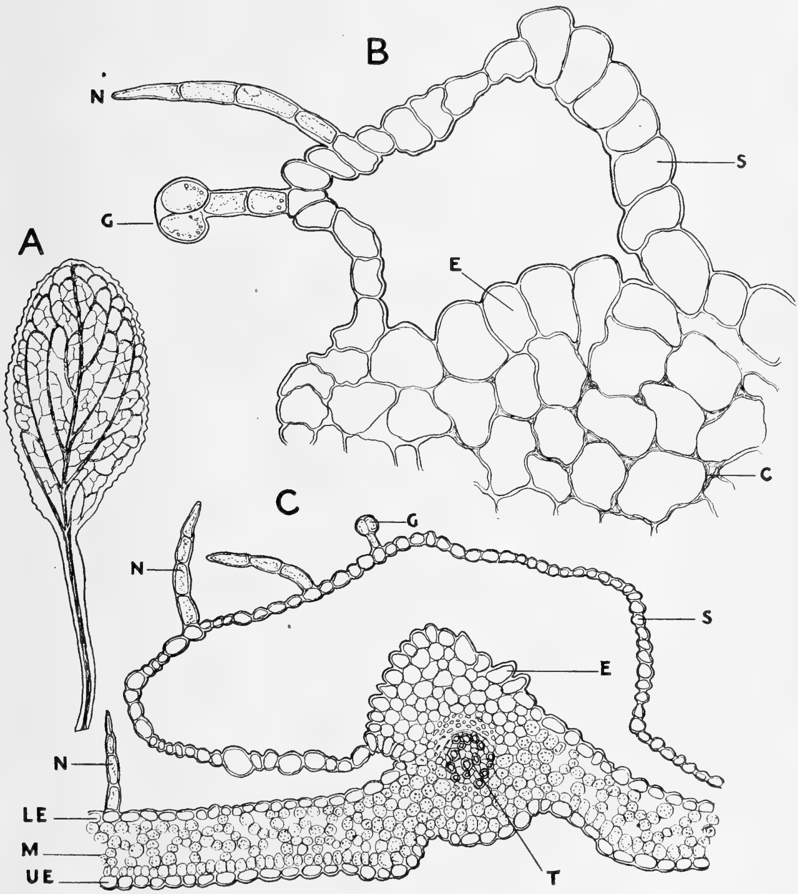
this is the practice of many discriminating pharmacists in the United States.

Of all the papers which have been published on digitalis, the one by Hartwich and Bohny [1] seems to me to be the most important from a pharmacognostical standpoint. The whole work is of a basic character and sets forth many observations showing variation in the structure of wild plants and those selected from cultivated varieties. These authors point out that among other things that the leaves of wild digitalis are usually more hairy, that the cells of the hairs are shorter and broader and that the cuticle, or outer walls, of the middle and lower cells of the non-glandular hairs are finely papillose. Vogl [2] has called attention to the fact that the end cells are occasionally either fine striated or slightly papillose. As a matter of fact the observations of both of these authors are correct. In regard to the number of cells making up these non-glandular hairs, Vogl states that they are mostly 3-celled, Hartwich and Bohny state that they are usually 2- to 4-celled and seldom 5- to 6-celled, and Greenish [3] records the fact that exceptionally they may be as many as ten cells long. While I have not been able to confirm Greenish's observation, I have seen specimens in which many of the hairs were 7 to 8 cells long, and I believe that his statement can be confirmed. Most authors agree that the head or glandular portion of the glandular hair consists of one or two cells but Hartwich and Bohny state that they are seldom 1- or 4-celled. The stalks of these glandular hairs are usually 1- or 2-celled. A most interesting observation is recorded by Hartwich and Bohny that in between the veins occur long glandular hairs with usually a 4-celled stalk and a 1-celled glandular head. These observations are all of the very greatest interest and should be borne in mind by students and practical workers in pharmacognosy.

The entire leaf of digitalis is very characteristic, being more or less elliptical and the lower portion extending into the petiole (Fig. 1). The margin is irregularly crenate but the most characteristic feature is the venation. From the central vein extend a number of prominent veins of the first order that diverge at angles of twenty to forty-five degrees, which serves to distinguish it from inula, in which the angles between the primary veins and the mid-rib are from sixty-five to nearly eighty degrees. The venation at the teeth is also considered by many authors [4] to be rather characteristic for digitalis. While the commercial drug will yield

in some instances nearly entire leaves it is for the most part made up of broken fragments and the microscopical study of these fragments is of the very greatest interest. There are a number of

FIG. 1.

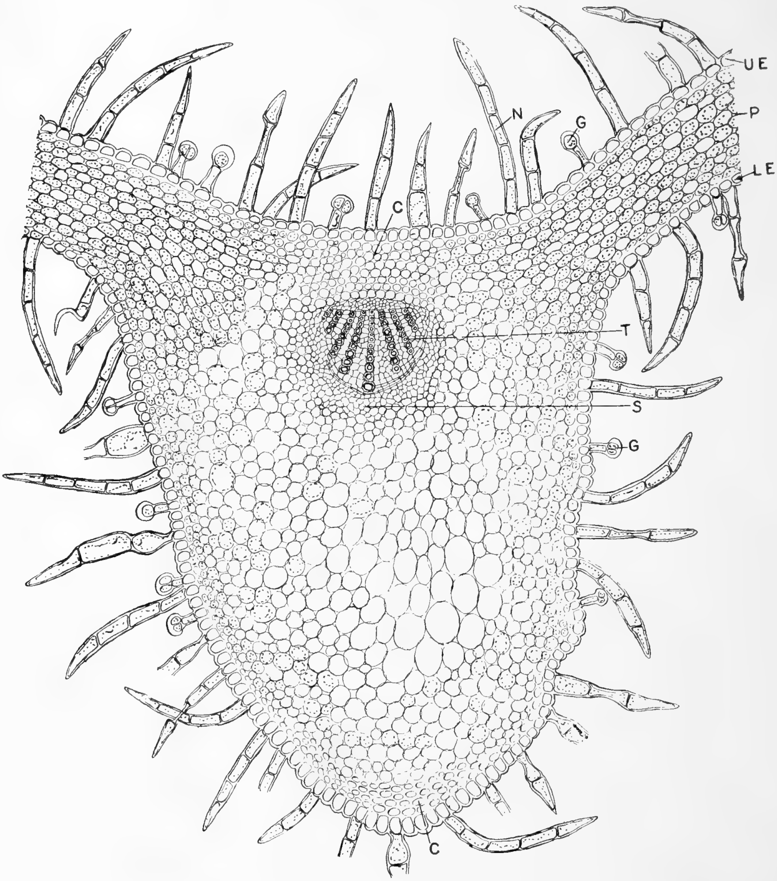


Digitalis: *A*, a typical leaf showing the winged or laminate petiole and the veins of the first order which diverge from the mid-vein at very acute angles. *B*, transverse section of portion of leaf showing the separated or additional epidermal layer (*S*); epidermal layer (*E*); glandular hair (*G*); non-glandular hair (*N*); collenchyma (*C*). *C*, transverse section near one of the veins showing considerable of the separated or extra epidermal layer (*S*); with two non-glandular hairs (*N*) and glandular hair (*G*); epidermal layer (*E*); lower epidermis (*LE*); chlorophyll layer (*N*); upper epidermis (*UE*); tracheæ or vessels (*T*).

characters in the anatomy of this leaf that might be studied, but I desire at this time to call attention only to certain variations of the hairs observed in different specimens of the commercial drug as also of the cultivated plants. It is well known that in the hairs

of many plants active principles are contained. For instance the volatile oils yielded by the Labiatæ are found in the glandular hairs of the plants comprising this family. The stinging hairs of the nettles are peculiar in structure and while of a non-glandular char-

FIG. 2.



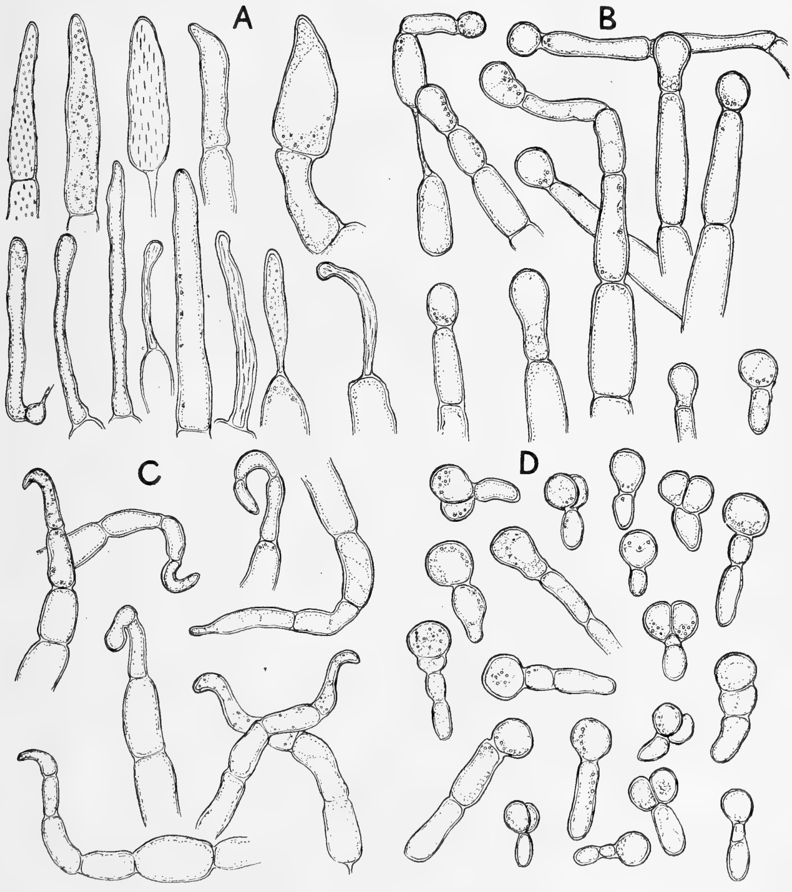
Transverse section of digitalis leaf, through one of the veins: *UE*, upper epidermis; *P*, chlorenchyma (mesophyll), containing chloroplastids; *LE*, lower epidermis; *G*, glandular hairs *N*, non-glandular hairs; *C*, collenchyma; *T*, tracheæ or vessels; *S*, leptome or sieve.

acter yet they contain irritating substances. Nothing appears to be known with regard to the nature of the secretory substances in the hairs in digitalis yet the fact that in certain specimens we find a preponderance of glandular hairs is suggestive that whether these substances are toxic or not or have any influence upon the action

of the cardiac substances it may be that the minute study of the hairs will throw some light on the variation in the drug.

As has been already stated there are two general types of hairs in digitalis, (1) non-glandular; (2) glandular. Usually the former

Fig. 3.



Various forms of hairs ot digitalis: *A*, various forms of apical cells; *B*, long stalked glandular hairs very common in leaves of cultivated plants; *C*, various non-glandular hairs showing crooked or bent apical cells; *D*, various forms of glandular hairs with short stalks.

occur in greatest number but the reverse is frequently the case, especially in cultivated garden varieties. In fact I have seen in certain instances the glandular hairs so numerous that I was inclined to think that the observations previously reported and the illustrations made were erroneous. The non-glandular hairs are usually

2- to 5-celled and vary in length from 145μ to 435μ. The cells are quite slender, being 9 to 13 times as long as broad. In other cases they are much shorter and broader, being twice as long as broad. The apex is usually obtuse or slightly rounded, and seldom acute. (Fig. 3, A.) In some specimens the end cell is characteristically curved or crooked (Fig. 3, C). Again the end cells of these long hairs may be nearly spherical and of a glandular character (Fig. 3, B).

The glandular hairs in the crude drug found on the market usually possess a short 1-celled stalk and a globular glandular head consisting of one or two cells (Fig. 3, D). In some specimens these are relatively few, or wanting entirely, while in other specimens they are quite numerous, being about 25 to the square millimeter. The greatest interest is in the long-stalked glandular hairs (Fig. 3, B), which, in some specimens of leaves from cultivated plants, largely replace the long non-glandular hairs. One may count upon a single cross-section about one half millimeter long, one complete non-glandular hair; three long-stalked glandular hairs; the basal cells only of nine hairs, and eleven short-stalked glandular hairs. The impression that one receives from seeing slides of this character is that the hairs of digitalis are chiefly of the glandular type.

One of the most unusual characters which has been observed in certain specimens of crude drug, has been the formation of an extra epidermal layer. It would be interesting to know the potency of preparations made from a drug of this kind. In presenting this paper at this time I have done so in order to call attention to the fact that the pharmacognostical study of this drug has by no means been exhausted. What is probably needed here is some statistical work in regard to the occurrence of the several types of hairs and their relative distribution in different specimens of the drug the pharmacological efficiency of which is being determined.

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[3] Henry George Greenish: The Microscopical Examination of Foods and Drugs, 1910, p. 136.

[4] A. Tschirch and O. Oesterle: Anatomischer Atlas der Pharmakognosie und Nahrungsmittelkunde, Lief. **15**, p. 319.

THE PREPARATION OF NEUTRAL SUSPENSION OF SALVARSAN.[1]

By George M. Beringer, Jr.

The directions for preparing the neutral suspension of salvarsan, as given in the literature accompanying the product, are, apparently, very simple and require but little time for carrying out; but therein lies a trap. The modified method given herewith has been found to yield a satisfactory product.

The apparatus and material required are very simple. There will be needed:

One or two beaker glasses (25 or 30 c.c.),
One cylindrical measure (10 c.c.),
Two thin glass rods with rounded ends,
One glass mortar (30 or 60 c.c.),
Three pipettes made from tubing of small diameter,
One or two ampoules (5 or 10 c.c. capacity),
One funnel with slender stem.

It has been found advantageous to keep these in a seamless tin box with tightly fitting lid. This is sterilized in a gas oven at a temperature of 200° C. for fifteen minutes and allowed to cool before using.

In addition, the following should be prepared, in previously sterilized containers:

50 c.c. 15 per cent. solution sodium hydroxide (in glass-stoppered bottle),
25 c.c. solution hydrochloric acid (1 part diluted HCl, 3 parts sterile water, in glass-stoppered bottle),
200 c.c. distilled water (contained in a flask and sterilized by boiling for 15 minutes),
Phenolphthalein test paper.

Salvarsan is sent into the market in sealed ampoules containing .6 Gm. The entire amount is generally made into suspension, the physician dividing the dose, if need be, when administering. It is, as you are probably aware, in the form of a hydrochloride. This is readily hydrolyzed by water, so that aqueous solutions contain free acid, which makes them objectionable for injection. While it is

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[1] Read at the meeting of the New Jersey Pharmaceutical Association, June 14, 1911.

soluble in alkaline solutions, they are exceedingly painful when injected; hence the need for a neutral suspension of the base itself.

The material having been prepared, as previously directed, the ampoule containing the drug is washed with water and, finally, with alcohol. This is necessary because they are generally badly smeared with glue. The ampoule is then opened and emptied immediately into the mortar. Fifteen or sixteen drops of the soda solution are added and mixed with the material. Then enough distilled water is added, drop by drop, to make a moderately thin paste. Great care must be taken, from this point to the end of the preparation, to thoroughly triturate the material. Every particle must be rubbed till a smooth, creamy mixture results. It is now to be tested for alkalinity by applying a small portion of the mixture, by means of one of the rods, to a piece of phenolphthalein paper. If not faintly alkaline add soda solution, drop by drop, with continued trituration, till it gives the reaction, adding sterile water, from time to time, if the preparation becomes too thick. Now the HCl solution is added, drop by drop, till the mixture just ceases to react upon the test paper. Great care must be taken to rub up any cheesy lumps that may form when the acid is added. More water is added and the mixture transferred to the graduated cylinder. The portions of the precipitate adhering to the sides of the mortar and the pestle are rinsed down with the aid of a glass rod and sterile water, dropped as needed, and added to that in the cylinder. Enough water is added to make the product measure 8 c.c. and the mixture transferred to the ampoule by means of the funnel. Two c.c. of water are now used to rinse the adhering material from the measure and funnel into the ampoule. The excess of stem is filed and broken from the ampoule, which is immediately sealed by a blow-pipe flame directed across the edge of the open tube till the glass is perfectly fused. After cooling, the container is shaken to insure mixing.

Many physicians make the injection at two sites, using the suspension in portions of 5 c.c each. For this purpose, a beaker glass will be needed in dividing the preparation. An extra beaker is provided because the operator frequently has immediate need of an extra vessel of some kind in the midst of his work.

It is better to have a large mortar than one too small, as the precipitate can be more easily rubbed smooth in the former. A porcelain dish as directed in the circulars is exceedingly unsatisfactory.

The hydrochloric acid is directed to be much more dilute than that originally used, as it has been found to give a lighter and a finer precipitate.

The suspension should not be prepared long before it is to be used. At least an hour, however, should be allowed for its preparation, and the operator should, under no circumstances, be hurried. The services of an assistant to handle the pipettes will materially shorten the time required.

Phenolphthalein paper is much more certain in determining the reaction than litmus. Red litmus does not change till a great excess of alkali has been added. Blue litmus is more sensitive but not so sharp in distinction as phenolphthalein. When neutral to the latter, the preparation slightly deepens the color of blue litmus. This seems to be the proper "end point," as, when more acid is added till just neutral to litmus, the suspension of the precipitate is not so perfect.

SOME THOUGHTS ON THE ACTION OF THE ENZYMES, WITH SPECIAL REFERENCE TO THE NATURE OF PEPSIN.[1]

By James E. Hancock.

Ever since the discovery of the enzymes, physiological chemists have tried to explain the transformations that occur under their influences and to systematically reason why these changes should be. One theory and then another has been suggested, each of which has been based upon certain peculiarity of reaction that has happened under the particular investigator's notice. The study is fascinating because metabolism generally is a physiological process that cannot be even approximately understood until the actions of enzymes are comprehended. Every problem in the growth and dissolution of plants and animals, and especially in the transferences of energy, is connected in some way or other with the action of enzymes. Plants, with very few exceptions, acquire their food from the soil and from the air. By the action of enzymes under favorable influences of light, heat and moisture, the organic materials that are thus absorbed are elaborated into complex compounds, consisting

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[1] Read at a meeting of the Maryland Pharmaceutical Association, June, 1911.

mostly of carbon, hydrogen, oxygen and nitrogen, and build up within themselves the sugars and vegetable proteids, which in turn are so necessary for the growth and maintenance of the animal kingdom. For a long time it was believed that all proteids were the products of vegetable life, but when the differences between the various complex albumins were studied, it was seen that the albumins found in animals were different from the albumins found in plants, and it is now known that no matter from what source the animal takes its food, the proteids have to be catalyzed before they are fit for its economy.

Digestion in itself is an extremely simple word, but it is very comprehensive, and few realize how much is included in the process. Some authorities consider enzyme actions as a part of the vital processes themselves, but others evidently cannot see beyond the material reactions that occur, until even in these days of advanced science no acceptable agreement is absolutely settled upon. The subject is necessarily a theoretical, indeed an obscure inquiry. In recent years a dynamic conception of the powers seems to be more and more acceptable and at least two advocates of such explanation would appear to approximate a reasonable theory for these processes. Naegeli assumes that catalysis is induced by vibratory action, and, apropos, it might be well to remind you that it is a generally accepted hypothesis to consider that the atoms of every molecule of matter are never at rest, but that they vibrate in a state of equilibrium which is consistent to the maintenance of its specific whole. It is supposed that the catalyzing agent—the enzyme—coming in contact with a body favorable to its action, communicates the vibrations of its atoms to the atoms of the molecules of the body that is being digested and breaks down their staple tension with a natural reduction of its complexes into other and simpler compounds. To get a better appreciation of what this atomic rearrangement may mean, we must remember that Grubler has estimated that the molecular weight of vitellin was 8848, from which was deduced the formula $C_{292}H_{481}N_{90}O_{83}S_2$, and that Sabanejeff has determined that the molecular weight of ovalbumin was 15,000. The atomic rearrangement in the changes that might occur in such complexes, especially if modified or interfered with by external factors and inequalities would suggest a procession of geometric possibilities. The dynamic law of Laplace and Berthollet "That an atom or molecule put in motion by any power whatever may communicate its own

motion to another atom or molecule in contact with it," would thus seem to acquire a special significance in the biochemistry of the enzymes and might account for the many catalyses and syntheses that occur in our own bodies and in growing plants and animals, under the actions of enzymes when influenced by the sun's rays and other favorable conditions. Ostwald's generalization practically implies the same character of action when he states that these changes are brought about by the increased activity of molecular movement.

Accepting either or both of these theories, even with modifications, they at least reconcile the transformations that may occur in the phenomena of digestion as a peculiar quality of the enzymes, the smallest particles of which may be assumed as being in a state of motion, a state which is communicated to the atoms of the material that is being digested and with which they are in contact, thereby causing the atoms of the molecules of this matter to change their position and rearrange themselves in new groupings. Supplement this induced rearrangement with the processes of either oxidation or hydration, dependent of course on the peculiar quality of the particular enzyme, and then carry this conception a little further and infer the action of disturbing external factors like heat or light, which are vibratory in their communications,—for it is entirely possible that the waves from these may intensify or abnormalize this existing process,—and the products that are thus formed must necessarily alter with the temperature and the other modifications of transformation in which the enzyme works, because the changes in the newer bodies are the result of these imparted energies and the atomic rearrangement that is thus brought about must stand in particular relation to the manner of the actions. During the past winter my attention was called to an auto-digestion of pepsin that could only be reconciled by this reasoning, and an experimentation of several months with recurring resultants under similar conditions has been an interesting problem. As we all know, pepsin is an extremely sensitive body, and the best chemists have never been able to analyze it. We all know it is a soluble, unorganized ferment that differs in its mode of action from living ferments such as yeast and bacteria, in that it possesses no power of self-nutrition and multiplication. Like all other animal extracts it is surrounded by the limitations that nature has placed upon it. It will bear an exposure to a prolonged low temperature without being injured, and it is active only in weak acid solutions, and then

when accompanied by two conditions—the presence of water and heat. Nature's economy provides that it shall be physiologically active at and about 100° F., while an exposure of its simple solution to a temperature of 130° F. will quickly destroy its proteolytic activity. Moreover, its digestive activity is always dependent on the medium in which it is exhibited. The U.S.P. requires that one grain of pepsin shall be able to digest 3000 grs. of coagulated egg albumin when suspended in a 0.2 per cent. HCl solution with water. By repurification this standard may be increased to a much higher potency; but even in the highest degree of purification that it has yet been obtained, it is at least in combination with nucleo-proteid bodies. These nucleo-proteids are combinations of nucleic acid with albumin. Recently several authorities have advanced the theory that the nucleo-proteids themselves are the enzymes. This is especially urged by Haliburton, and Pekelharing has practically arrived at the same conclusion and suggests that the nucleo-proteid is probably the zymogen of the enzyme. This hypothesis is strengthened by the observations of McCallum, who showed that in nature the nucleus initiates the process of secretion and excretes some material into the cytoplasm which then undergoes further changes and ultimately enters into the zymogen, if indeed it does not actually form the principal part of it. Nencki and Sieber also state that pepsin contains nucleo-proteid and conclude that the zymogen—pepsinogen—is converted into pepsin by combining with the nucleo-proteid of the cell. The practical results of pepsin digestion of nucleo-proteids have been frequently demonstrated. Although they are much more resistant to hydrolysis than the true albumins, nevertheless under a prolonged peptic digestion, the nucleo-proteids are split into nucleins, being new compounds of nucleinic acid and protein fractions.

A series of experiments in which pepsin and its natural associates were the only possible albuminous quantity present, in an acidulated solution under the action of heat and electric light for ten days, have given the following results: A precipitation of modified nuclein that is insoluble in the acid medium and a propeptone moiety that remains dissolved in the solution. I wish that I were prepared at this time to give you the ultimate results, but certain conditions will not permit. The purpose of this paper is only to urge that pepsin solutions should be kept in a cool, dark place, because of their sensitiveness to heat and light.

A NEW VEGETABLE ADULTERANT.

(OUTER LAYERS OF THE PERICARP OF THE FRUIT OF JUGLANS REGIA L.)

By Henry Kraemer.

At the Pharmaceutical Meeting of the Philadelphia College of Pharmacy held November 16, 1909, Mr. E. H. Gane exhibited a sample of "vegetable shells," which he stated were imported probably for the purpose of replacing walnut shells, olive pits, etc., owing to the ease with which these latter products can now be detected when used as adulterants. (See *Am. Jour. Pharm., 81,* p. 597, December, 1909.)

A preliminary examination of the sample showed that it was composed of the pericarp of some fruit. I then gave the sample to one of my students, Mr. Peter Amsterdam, to study microscopically and in comparison with the pericarps of similar fruits in our collection. This study showed that the material consisted of the hulls, or outer layers of the pericarp, of the fruit of *Juglans regia,* or English walnut, the nuts of which are common in the markets as an article of food.

The hulls (outer portion of the pericarp) of the fruit of *Juglans regia* have been used in the fresh and green condition in medicine, and are described in foreign works under the name of *Cortex Fructus Juglandis* (*Cortex nucum Juglandis viridis. Grüne Walnussschalen. Brou de noix*). The hulls are described by Vogl in his Pharmacognosy, and a rather extensive article on their histology is given by Hartwich in the *Archiv der Pharmacie, 66,* p. 325 (1887).

Macroscopic Characters.—The dried hulls, or "shells," consist of pieces or fragments composed for the most part of the outer layers of the pericarp, *i.e.,* the epicarp and sarcocarp. The pieces are more or less irregular, involuted, shrivelled, vary from 5 to 35 mm. in diameter, and break with a short fracture. Some of the pieces are marked by the stem-scar or still have attached to them portions of the stem. Externally, the epicarp, or outer layer, is rather smooth, though coarsely wrinkled, marked by numerous small dots, and varies in color from light to dark brown. The sarcocarp, or inner layer, is somewhat spongy, dark brown or black-

ish-brown in color, and more or less fibrous, due to the shrinkling of the parenchyma from the fibrovascular bundles.

The taste of the hull is markedly acid and somewhat bitterish, but the odor is not very pronounced or characteristic.

Microscopic Characters.—The epicarp shows the presence of numerous broadly elliptical stomata (Fig. A) which are from 50 to 70 microns in length; the opening between the guard-cells is large, and sometimes irregular in outline, or the guard cells may be separated along the adjoining walls, due to the unequal development of the tissues. The blackish-brown spots, which mark the outer surface of the epicarp are made up of tannin-containing cells which appear to be under the influence of a local stimulus of some kind, the area affected being 0.2 or 0.3 mm. in diameter. The epidermal cells are more or less polygonal, the cuticle being from 2 to 5 microns thick (Fig. B, e). Beneath the epidermis are two to three rows of tabular cells, usually containing a reddish-brown or tannin-containing sap (Fig. B, c); beneath these sub-epidermal cells is a continuous ring or zone (Fig. B, s) made up of three or four layers of stone cells, the walls of which are strongly lignified, lamellated, and finely porous. The cells vary from tabular to irregular, and may or may not contain a reddish-brown tannin-like substance, the tannin being in the cells of the specialized areas already described.

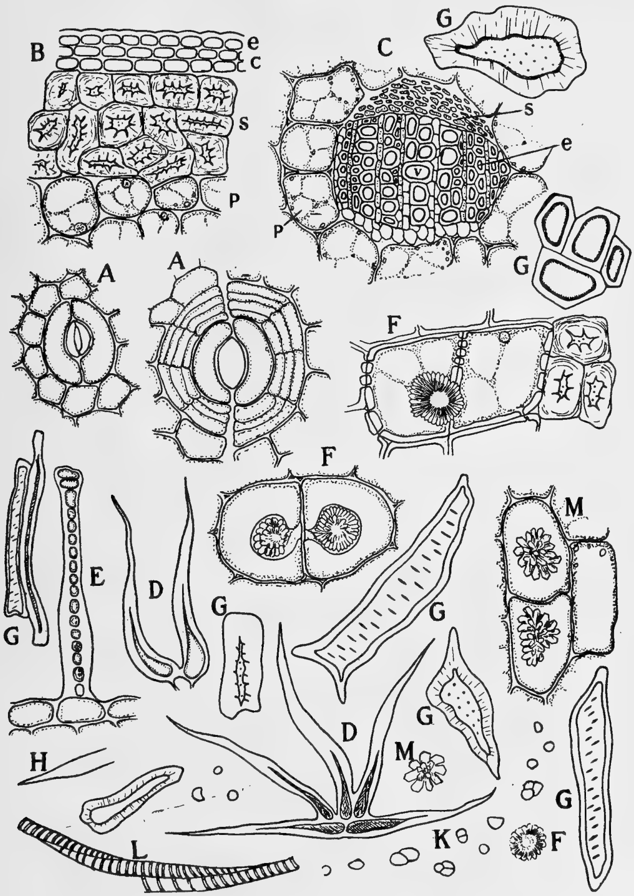
Beneath this zone of stone cells occur the tissues of the sarcocarp proper (Fig. B, p). This portion consists of parenchyma and fibro-vascular tissue. The cells of the parenchyma contain small starch grains and occasionally rosette aggregates of calcium oxalate which vary in diameter from 25 to 40 microns, and sometimes may be found in large numbers in the parenchyma cells adjoining the fibrovascular bundles.

The parenchyma cells of the sarcocarp of the young fruits have very thin walls, but in the older fruits the walls of very many of the cells become lignified and have large oblique pores. The tracheæ are in radial rows two cells wide separated by medullary rays one cell wide. They are usually spiral.

At both the apical and basal portions of the fruit occur curved, spear-shaped, unicellular, non-glandular hairs (Fig. D) resembling those found in the pericarp of the cereal grains, but distinguished from the latter by the fact that they are frequently united to form stellate groups resembling

those of kamala and those occurring on the leaves of hamamelis. The contents may be nearly colorless or consist of a reddish-brown tannin-like substance. There are also

Fig. 1.



Pericarp of fruit of *Juglans regia:* *A*, stomata of epicarp; *B*, cross-section of pericarp; showing epidermis (*e*), cells with reddish-brown contents (*c*), sclerotic cells (*s*), parenchyma (*p*), containing protoplasm and starch grains; *C*, mestome strand of the sarcocarp showing vessels (*v*), libriform (e), leptome (*s*), parenchyma containing protoplasm and starch (*p*); *D*, non-glandular hairs from the apical and basal portions of fruit; *E*, glandular hairs from base of fruit similar to those found in large numbers on the surface of the butternut (*Juglans cinerea*); *F*, rosette-aggregates resembling the membrane crystals of Rosanoff; *G*, sclerotic cells found in the powder; *H*, fragment of non-glandular hair; *K*, starch grains from 2 to 10 u in diameter; *L*, tracheæ with annular markings; *M*, calcium oxalate crystals.

present, usually at the base of the fruit, and also on the stems, when these are present, long-stalked glandular hairs (Fig. E) similar to those covering the fruit of *Juglans cinerea* (Butternut).

While the stalk is long and multicellular in the hairs of both species, the glandular head in the hairs of *Juglans regia* appears for the most part to consist of one or two cells, whereas in *Juglans cinerea* it is usually multicellular, resembling the glandular heads of the hairs of the *Labiatæ*.

In the parenchyma cells of the basal portion of the hull there are a large number of rosette aggregates or spherites of crystals resembling crystals of calcium oxalate (Fig. F). These aggregates are more or less hollow, frequently attached to the cell-wall, sometimes more or less enclosed by the cell-wall, and thus resemble the membrane crystals of Rosanoff (see Kraemer's Botany and Pharmacognosy, 4th ed., p. 171). These aggregates differ from those found in the stem, which are the typical rosette aggregates of calcium oxalate, and are deserving of special study.

Characteristics of the Powder.—The color is dark brown or blackish-brown, the odor faint, and the taste distinctly acid and slightly bitter. The most characteristic elements of the powder are the stone cells (Fig. G), some of which contain only air, thus resembling those of the olive pit, and some of which have a reddish-brown content. There occur besides fragments of the stalks of the glandular hairs (Fig. D), fragments of the non-glandular hairs (Figs. D and H), small starch grains (Fig. K), the two types of rosette aggregates of calcium oxalate crystals (Figs. F and M), and large, thin-walled somewhat shrunken parenchyma cells, many of which contain either small starch grains or reddish-brown masses, or cells with rather thick walls having large simple pores and being more or less lignified, approaching stone cells. These latter sometimes contain the Rosanoff crystal aggregates already mentioned.

When the hulls of *Juglans regia* are treated with water the solution soon shows a reddish-brown color which becomes much deeper on the addition of aqueous solutions of the alkalies. The aqueous extract of black pepper hulls, and black walnut shells (endocarp) has a color similar to that of the hulls of *Juglans regia* and behaves similarly toward solutions of the alkalies. The aqueous extract of pecan shells (endocarp) is of bright red or cherry red color, but becomes on the addition of alkalies of a dark reddish-brown color similar to that of the extract of the hulls of *Juglans regia.* Cloves give a reddish-yellow aqueous extract which becomes deep red on the addition of solutions of the alkalies. The aqueous ex-

tracts of the following, are either nearly colorless or range from a pale yellow to a pale yellowish-red, or pale olive green; and are not turned to a dark reddish-brown on the addition of alkalies: Black pepper, white pepper, Ceylon cinnamon, Cassia cinnamon, Saigon cinnamon, pimenta, ginger, English walnut shells (endocarp), olive endocarp (olive pits), peanut shells, Brazil nut shells (seed coat), and butternut shells (endocarp).

HARVEY WASHINGTON WILEY.

On Thursday, July 13th, the readers of the daily press were surprised to learn that the Committee on Personnel of the U. S. Department of Agriculture, consisting of Assistant Secretary Willet M. Hays, Solicitor George P. McCabe, and Chief Clerk C. C. Clark, had been "investigating a charge that Dr. Wiley and Dr. Kebler have exceeded their authority under the law in employing Dr. Rusby, and have recommended that Dr. Wiley be permitted to resign; that Dr. Kebler be put in a place where he will no longer have power to make recommendations as to employment of experts, and that Dr. Rusby be dismissed."

Scarcely anything short of an attack upon the country by a foreign foe could have so stirred the hearts of the American people generally. Dr. Wiley has published so many papers, has delivered so many public addresses, and has himself been the subject of so many interviews, that he, as a matter of fact, has been in the "limelight" continually. Furthermore, he is so genial, he is such a good speaker, he is so considerate of the welfare of the people that he may very properly be termed one of "America's leading citizens." Since the passage of the Federal Pure Food and Drugs Act he "has wielded more power than almost any other subordinate official of the Department of Agriculture. He was the prime mover in all the pure food legislation that has been enacted, and has been charged with the execution of the law under the direction of the Secretary of Agriculture. Practically single-handed, he has waged a vigorous fight against the adulteration of foods entering into domestic and foreign commerce and has presented an uncompromising front to every attempt to evade or let down the strict letter of the law."

To prepare a sketch of Dr. Wiley and his work would be to write a volume. Briefly then, Dr. Wiley was born on October 18, 1844, near Kent, Jefferson County, Indiana. In 1863 he entered the freshman class of Hanover College, graduating A.B. in 1867. Entering upon the study of medicine in 1868, he graduated M.D. from the Indiana Medical College in 1871. During his medical course he was instructor in Latin and Greek at Butler College. In 1872 he entered the Lawrence School of Harvard University, graduating B.S. in 1873. He was Professor of Chemistry at Butler College in 1873-4, and from 1874 to 1883 he filled the position of Professor of Chemistry at the Agricultural College of Indiana at Purdue. During this period he had leave of absence for the year 1878-79 and studied in Germany. He was State Chemist of Indiana from 1881 to 1883; was made Chief of the Division of Chemistry, U. S. Department of Agriculture in 1883, which position he held up to 1901, when he became Chief of the Bureau of Chemistry, which position he holds at the present time.

The record of Dr. Wiley's connection with the evolution of the Federal Food and Drugs Law and legislation concerning Foods and Drugs in the United States, is, indeed, a stimulus to any young man with a laudable ambition. It is the successful record of a man with an ideal, who has worked indefatigably until his ideal became a reality. And, furthermore, like other men who have achieved great things for their countrymen, we find a cabal seeking to humiliate him. It is now just a quarter of a century ago that Dr. Wiley, as Chemist, submitted to Hon. N. J. Colman, then Commissioner of Agriculture, the first Bulletin (No. 13) on Foods and Food Adulterants. This Bulletin deals with dairy products only, but was rapidly followed by other detailed scientific studies on other products, as spices and condiments, fermented alcoholic beverages, lard, baking powders, sugar, molasses and syrups, tea and coffee, canned vegetables, cereals and preserved meats. At the very beginning Dr. Wiley realized that the support of the public who eat the food would be vital to the propaganda, for in 1889 he submitted Bulletin 25 of the Bureau of Chemistry to the Hon. Jerry M. Rusk, then Secretary of Agriculture, entitled "A Popular Treatise on the Extent and Character of Food Adulteration." In submitting this report by Special Agent Wedderburn, Dr. Wiley said:

"The object of the present bulletin is wholly distinct from that pursued in Bulletin No. 13. The investigations, of which the present bulletin is the

result, were undertaken for the purpose of collating in popular form well authenticated facts respecting food adulteration, in order that the people and Congress might have at least a general view of the evil which it is hoped Mr. Wedderburn's work may help to remove."

Mr. Wedderburn states in this Bulletin: "Enough will be found, I am convinced, in the pages of the following report to emphasize in the strongest manner the necessity for such national legislation as was sought during the last session of Congress by Messrs. Conger and Laird of the House Committee on Agriculture, as expressed in their very able report, as submitted to Congress by order of that committee."

Some of the data in these pioneer reports are especially interesting in view of later developments. "Glucose is probably the leading adulterant on the market. It is largely used in syrups, low-grade sugars, jellies, and cheap confections. Druggists, wholesale and retail, had none, but with singular unanimity referred the inquirer to the candy manufacturers who, to a man, knew nothing of the commodity. Parenthetically, a specimen of taffy of another kind, abstracted from an inviting pile, yielded 79 per cent. of glucose on analysis." (Beckwith, Ohio State Board of Health.) Pickles, greened with sulphate of copper, adulterated spices, vinegars, canned foods, maple products, etc., all clamor in these pages for the attention that they have recently received in the notices of court judgments issued from the Department of Agriculture.

One bill followed another, and in every Congress from the Fiftieth (1887) on a food bill was reported to each House. As chairman of the Committee on Legislation of the National Pure Food and Drug Congress, called in 1898, and as a witness every year before the Congressional committees considering these bills, Dr. Wiley has been indefatigable in his advocacy of pure food and drugs for the people, backing up his views with the scientific work of the Bureau of Chemistry on the one hand, and with popular education on the other.

The study of imported foods was begun in 1898. Samples of a number of classes of foods were procured from the Custom officers at the various ports of entry and their quality and composition compared with similar food products purchased upon the open market alleged to be imported. The results were very interesting. On March 3, 1903, Congress in the Appropriation Act authorized the Bureau of Chemistry to supervise the importation of food

products. This law became effective July 1, 1903. The act authorizing this work reads as follows:

"To investigate the adulteration, false labelling, or false branding of foods, drugs, beverages, condiments, and ingredients of such articles, when deemed by the Secretary of Agriculture advisable, and report the result in the bulletins of the Department; and the Secretary of Agriculture, whenever he has reason to believe that such articles are being imported from foreign countries which are dangerous to the health of the people of the United States, or which shall be falsely labelled or branded, either as to their contents or as to the place of their manufacture or production, shall make a request upon the Secretary of the Treasury for samples from original packages of such articles for inspection and analysis, and the Secretary of the Treasury is hereby authorized to open such original packages and deliver specimens to the Secretary of Agriculture for the purpose mentioned, giving notice to the owner or consignee of such articles, who may be present and have the right to introduce testimony; and the Secretary of the Treasury shall refuse delivery to the consignee of any such goods which the Secretary of Agriculture reports to him have been inspected and analyzed and found to be dangerous to health or falsely labelled or branded, either as to their contents or as to the place of their manufacture or production, or which are forbidden entry or to be sold, or are restricted in sale in the countries in which they are made or from which they are exported. . . . ." (Section of Appropriation Act of March 3, 1905.)

The same act provides for an investigation of food preservatives in the following language:

"To enable the Secretary of Agriculture to investigate the character of proposed preservatives and coloring matters, to determine their relation to digestion and to health, and to establish the principles which should guide their use."

The results of the work were so satisfactory that laboratories were established in New York, San Francisco, Boston, Philadelphia, Chicago and New Orleans.

The Federal Food and Drugs Act was passed on June 30, 1906, and became effective January 1, 1907. The enforcement of this law was placed in the hands of the Bureau of Chemistry. Dr. Wiley was one of the three members of the special committee appointed to draw up regulations for the enforcement of the act. These regulations with minor changes in a few instances are still in force. Under this act the port laboratories referred to above remained in force, and numerous others were provided for at various ports of entry, as, for example, Savannah, Seattle, St. Louis, Detroit, etc. Thousands of foods and drugs have been examined under this act

and hundreds of successful prosecutions made. These prosecutions include some of the most flagrant frauds perpetrated on the public. For example, some of the so-called cancer cures, consumption cures, drug addiction cures, cocaine traffic, soothing syrups, etc. Dr. Wiley, through the drug division, has co-operated with the Post Office Department for the purpose of denying the privileges of the mails to numerous medicinal frauds, which is accomplished by the issuing of fraud orders by the Postmaster-General, after being satisfied that the parties engaged in the business are obtaining money by false and fraudulent promises and representations.

It will be seen that absolute unity of purpose and principle runs through Dr. Wiley's whole record, there is no wavering or hedging at any point. He has not only had the confidence of the people, but also of his colleagues engaged in scientific work. He was elected President of Section C of the American Association for the Advancement of Science in 1886; was Secretary of the Council of the American Association for the Advancement of Science in 1889, and General Secretary in 1891. He became President of the American Chemical Society during 1893–4, and was President of the Indiana Academy of Science in 1902. He was selected as the delegate from the United States to the second, third, fourth and fifth meetings of the International Congress of Applied Chemistry. He was a member of the Jury of Awards at the Universal Exposition at Paris, 1900. He also has been Professor in Agricultural Chemistry, Graduate School, Columbian University, since 1899. He received a medal of the first class of the Physicochemical Academy of Italy in 1908. He was made Chevalier Merite Agricole in 1900 and Chevalier Légion d'Honneur in 1909. He was the Honorary President of the International Congress for the Repression of Adulteration in Geneva in 1908. In May of last year he was elected the President of the U. S. Pharmacopœial Convention. He is the author of a number of books and has published some 60 government bulletins and 225 scientific papers.

This series of facts relating to the career of Dr. Wiley shows that he is a man who gets results. He is strong in physique and is a prodigious worker. That he knows how to get things done is not only manifest in the enactment of the Federal Pure Food and Drug Law, but in the enforcement thereof. The annual reports of the Bureau of Chemistry are simply staggering. In addition to the extensive investigations on important food and drug products car-

ried on by the department in Washington during the year 1910, and also in examination of about 20,000 samples, the following tabulated statement of the activities of the twenty-one branch laboratories is of interest as indicating in a general way the extent of the work done:

Laboratory	Imported samples			Hearings conducted	Interstate samples		Miscellaneous samples	Total samples analyzed
	Legal	Illegal	Floor-inspection samples		Legal	Illegal		
Boston	460	295	12,404	674	744	270	140	1,909
Buffalo	76	29	33	159	146	231	41	523
Chicago	173	125	2,572	365	658	686	42	1,684
Cincinnati	19	4	28	239	1,157	228	1	1,409
Denver	11	...	11	160	395	175	44	625
Detroit	52	4	92	359	151	144	31	382
Galveston	59	22	365	116	192	144	44	461
Honolulu[1]	272	144	677	131	...	...	8	424
Kansas City	...	...	...	103	125	127	...	252
Nashville	...	...	...	157	191	65	...	256
New Orleans	95	84	2,891	197	148	108	76	511
New York	2,382	1,632	47,821	1,779	124	297	504	4,939
Omaha	...	...	3	69	239	110	100	449
Philadelphia	569	183	5,250	293	41	114	48	955
Pittsburg	47	54	227	197	162	216	55	534
Portland	248	106	4,636	137	112	143	46	655
St. Louis	14	6	239	295	365	281	99	765
St. Paul	74	13	233	85	136	55	4	282
San Francisco	237	209	8,100	491	469	375	153	1,443
Savannah	65	40	26	159	105	51	19	280
Seattle	277	137	1,657	113	50	41	168	673
Total	5,130	3,087	58,726	6,278	5,710	3,861	1,623	19,411

[1] Owing to death of its chief, this laboratory was closed during the month of June; report is total for eleven months.

Dr. Wiley is not only a man of great executive ability but possesses a marvellous amount of patience. The Food and Drugs Act of June 30, 1906, became effective on the first day of January, 1907, and yet in his annual report to the Secretary of Agriculture on November 13, 1907, Dr. Wiley says:

"Previous to this date (January 1, 1907) it was necessary to carry out the provision of the law providing for the establishment of regulations. To this end a committee, consisting of H. W. Wiley, Chief of the Bureau of Chemistry, S. N. D. North, Director of the Bureau of the Census, Department of Commerce and Labor, and James L. Gerry, Chief of the Division of Customs, Treasury Department, acting for the Secretaries of Agriculture,

of Commerce and Labor, and of the Treasury, respectively, prepared a set of tentative regulations. Great care was exercised in *the preparation of these regulations, not only that the provisions of the law should be fully executed, but also that there should be no unnecessary annoyance or burden placed upon the trade.* It was deemed advisable before the promulgation of these regulations to hold public hearings in order to obtain the opinions of manufacturers and dealers. To this end, hearings were held in New York during the month of September, 1906, and were continued for a week. Upon the adjournment of these hearings the committee met frequently for the purpose of formulating the regulations, which were finally completed, signed, and promulgated on October 17, 1906, as Circular 21 of the Secretary's Office. As soon as these regulations were published a great flood of correspondence poured into the Bureau of Chemistry, necessitating a large increase in the clerical force. At the same time, also, arrangement was made for increasing the chemical force, to be ready for the increased activities of the work incident to the enforcement of the law on the first of January, 1907.

"Between January 1 and June 30, 1907, the personnel of the Bureau of Chemistry was more than doubled, the increase being divided between the clerical force, chemical assistants, and the corps of inspectors. The work incident to the enforcement of the law proved to be of far greater magnitude than had been anticipated, *and up to July 1, 1907, no actual prosecutions under the interstate feature of the law had been instituted. During this time, however, a much more rigorous execution of the law relating to imported foods was established.* This was possible because under the previous laws the machinery for the inspection and analysis of the imported foods had been already well organized. The only change which was made, therefore, in this service was to transfer the execution of the law from the clause in the appropriation bill provided therefor and place it directly under the Food and Drugs Act of June 30, 1906.

"It will not be out of place, however, to mention in this connection that, although up to the 1st of July no actual cases had been instituted in the courts under the Food and Drugs Act, *the moral effect of the act was apparent in every branch of trade connected with the food industry. One of the most gratifying features of this preliminary activity has been the almost unanimous support accorded by the trade to the principles of the act. In the majority of cases manufacturers of food products, as well as dealers therein, have expressed their cordial support of the act and offered their hearty collaboration in securing its enforcement. The importance of this fact can not be overestimated, since the difficulties of enforcing an act, if the entire food trade were opposed to it, would be practically insuperable."* [1]

I think it was the poet Whittier who said: "Young man, if you would be truly successful ally yourself with an unpopular but righteous cause." This was what Dr. Wiley did many years ago in the cause of pure foods and drugs, and in the prime of his life the dream of his youth has become a law. But he was not to stop

[1] *Italics by Editor.*

here, for he was charged with the difficult task of seeing that this law was judiciously administered. After five years it may be safely said that the fruits of his labors are enjoyed, not only by the general public, but have redounded to the advantage of the 98 per cent. of ethical business men in the United States as well as abroad.

HENRY KRAEMER.

AMERICAN PHARMACEUTICAL ASSOCIATION.

PHILADELPHIA BRANCH.

A special meeting of the Philadelphia Branch of the A.Ph.A. was held at the Philadelphia College of Pharmacy, in connection with the officers or representatives of a number of other associations and the colleges of pharmacy in Philadelphia, to take some action which would counteract the recommendation of the Committee on Personnel of the U. S. Department of Agriculture that Dr. Wiley "be permitted to resign" (see page 381). The President of the local branch, Dr. I. V. Stanley Stanislaus, presided, and asked Professor Kraemer to read the resolutions which he had prepared to be endorsed, if the members present so desired, and sent to President Taft. The following are the resolutions, which were read and unanimously adopted:

PHILADELPHIA, PA., July 17, 1911.

To the Honorable William H. Taft,
President of the United States.

The following preamble and resolutions, passed at a special meeting of representatives of the organizations named, are respectfully submitted for your consideration:

WHEREAS, We, the officers and representatives of the Pennsylvania Pharmaceutical Association, Philadelphia Association of Retail Druggists, Philadelphia Branch of the American Pharmaceutical Association and its Scientific Section, Philadelphia Branch of the American Chemical Society, The Philadelphia College of Pharmacy, Department of Pharmacy of the Medico-Chirurgical College and Department of Pharmacy of Temple University, in special meeting assembled, having learned that the Committee on Personnel of the United States Department of Agriculture has recommended that Dr. Harvey W. Wiley, Chief of the Bureau of Chemistry of that department, "be permitted to resign"; and

WHEREAS, The services rendered by Dr. Wiley, as chief chemist have been eminent and have revealed a progressive and liberal spirit, and have

furthermore been of great benefit not only to the agricultural interests of the country but to the American people as a whole; and

WHEREAS, Dr. Wiley was the chief promoter of the Federal Pure Food and Drugs Law, one of the most beneficent measures ever enacted by Congress, and has been untiring and fearless in carrying out its provisions since its adoption; and

WHEREAS, The drug trade generally throughout the United States has always had confidence in the integrity and ability of Dr. Wiley, and have endeavored in every manner to support his efforts in the wise and judicious administration of the Pure Food and Drugs Law; therefore, be it

Resolved, That we heartily endorse and commend the work which Dr. Wiley has done in securing the enactment of the Pure Food and Drugs Law, and in making the law effective since its adoption, which action has had a most wholesome influence upon the practice of pharmacy, both retail and wholesale; and furthermore, be it

Resolved, That we earnestly deplore any movement which would either cause Dr. Wiley to resign at this time, which it seems to us would be little short of a public calamity, or tend to hamper him in his efforts to make this law effective and thus render it a dead letter.

Brief addresses were made by the following: Mr. Ambrose Hunsberger, Prof. C. B. Lowe, Mr. Christopher Koch, Mr. C. Mahlon Kline, Mr. Joseph W. England, Dr. William D. Robinson, Prof. C. E. Vanderkleed, Mr. Wm. A. Carpenter, Prof. H. B. Morse, Prof. John R. Minehart, Mr. Wm. E. Lee, Mr. Wm. L. Cliffe, Mr. Charles Rehfuss, Mr. William McIntyre and Mr. Wm. Martindale.

BOOK REVIEWS.

ESSENTIALS OF VOLUMETRIC ANALYSIS. An introduction to the subject, adapted to the needs of students of pharmaceutical chemistry. By Henry W. Schimpf, Ph.G., M.D., Professor of Analytical Chemistry in the Brooklyn College of Pharmacy. Large 12mo. xiv + 358 pages, 61 figures. New York: John Wiley & Sons. Cloth, $1.50.

This is the second edition of this book. It has been largely rewritten and makes a good impression partly for the reason that emphasis is placed upon an understanding of the principles underlying volumetric analysis. The author has not adopted the easy method of clipping processes from the U. S. Pharmacopœia, but has

conscientiously digested the subject, and presented the results in a very creditable manner. The volumetric methods are arranged in a systematic manner and comprise alkalimetry, acidimetry, precipitation, analysis involving the use of silver nitrate, sodium chloride and potassium sulphocyanate. The oxidation methods involve the use of potassium permanganate, potassium dichromate and iodine. The reduction methods involve the use of sodium thiosulphate, arsenous acid and stannous chloride. There are also given concise descriptions of methods for assaying alkaloidal drugs, phenol, oils, sugars, formaldehyde, and alcoholic liquids, together with a few simple gasometric analyses, such as a pharmacist may find useful. The book ought to be in the hands of pharmacists generally, and we believe that even students in chemistry would find the book of considerable value.

History of the Vegetable Drugs of the Pharmacopœia of the United States. By John Uri Lloyd, Pharm. M. This is Bulletin No. 18 of the Lloyd Library of botany, pharmacy and materia medica, published by J. U. and C. G. Lloyd, Cincinnati, Ohio.

The volume at hand brings to mind the quarterly publication entitled "Drugs and Medicines of North America," which was published by the Lloyd Brothers in 1884. This was an ambitious undertaking, and to pharmacists it was much like Gray's Flora of North America to botanists. Probably no two men were by nature and inclination as well as literary ability so well qualified to give a record of American medicinal plants including the history, botany, chemical constituents and pharmaceutical preparations as these authors. This work was suspended when No. 5 of Volume II was published in 1887. A few years later it was proposed largely as a result of the interest taken by Professor Flückiger in the subject, that a "Pharmacography of North American Medicinal Plants and Drugs" should be written conjointly by himself and Professor Lloyd. The death of Flückiger, however, terminated the enterprise, bringing to Professor Lloyd, as we can well understand, "one of the greatest disappointments of his life."

In the present volume the history of the vegetable drugs of the U.S.P. Eighth Revision are given. "Only enough is chronicled of each drug's beginning to point to the peoples or individuals who introduced it to medicine and pharmacy, no attempt being made to

follow the details of subsequent manipulations." A bibliography with over 700 references to books, monographs and articles completes this Bulletin. There are also included portraits of Dr. Rice and Professor Remington, the former being elected chairman of the Committee of Revision in 1900 and the latter Dr. Rice's successor.

This Bulletin contains very much valuable information and will not only be found useful as a reference book by the student but makes interesting reading. A rather curious omission is noted in the bibliography. While certain American medical journals are cited, the AMERICAN JOURNAL OF PHARMACY is not mentioned, although some references to Bastin's articles (as on p. 91) are given in the text and other references are made to this JOURNAL throughout the Bulletin. The same thing may be said of other publications, although fortunately the references are given in the text in connection with the discussion of the individual drugs. So that as a matter of fact the bibliography is much more extensive than would appear from the figures given.

HANDBUCH DER PHARMAKOGNOSIE von A. Tschirch. Lief. 22–25. Leipzig: Chr. Herm. Tauchnitz. Each Lieferung 2 marks.

In these brochures we have a continuation of the class of subjects introduced in the preceding Lieferungen and include the following: starch-yielding substances; inulin containing drugs; drugs containing triticin; polysaccharides occurring in membranes of plants as cellulose, lichenin substances, pectinous substances, mucilages and gums. The same high character of work is maintained and it is truly remarkable that it has been possible for Professor Tschirch to write so many original papers and publish at the same time this epoch-making book. It should be in the library of every pharmaceutical and medical school as well as in manufacturing laboratories. Of course pharmacognosists and food analysts are securing the Lieferungen as they are published, but owing to the general interest in many of the subjects treated, particularly by reason of the excellent illustrations, the latter half of the work might well be placed in technical schools, universities, and museums where raw materials are exhibited and studied, as well as employed for demonstration in connection with lecture courses. Botanists will find this work of Tschirch's like that of Wiesner's "Die Rohstoffe," and Czapek's "Biochemie der Pflanzen" of much value as a reference book.

Pharmakognostische Rundschau über das Jahr 1910. Bericht über die im Jahre 1910, periodisch erschienene Literatur aus dem gebiete der Drogenkunde und ihrer Hilfswissenschaften, von Prof. Dr. W. Mitlacher, Dr. O. Tunmann and Dr. M. Winckel. 1911. Verlag der *Pharmazeutischen Post,* Dr. Hans Heger, Wien, 1; Pestallozzigasse 6. $2.00.

It is rather stimulating to pharmacognosists to find that a volume of nearly 300 pages, containing a digest of the important pharmacognostical literature for 1910 is available in this form. In addition to some 50 pages in which are considered some general articles of a historical and special nature, abstracts of the various drugs are given under the respective plant families, and the latter are arranged in alphabetical order. The general disposition of the matter is such that it forms a very handy reference work. The abstracts are quite full and, having been prepared by specialists, contain all of the essential features. It is hoped that the sales of this work will be sufficiently great to warrant a continuation of its publication. When we consider the importance of the subject and the excellence of the work done, it would seem unnecessary to say that it is indispensable and should be in the libraries of our colleges and schools of pharmacy, and of botanists, pharmacognosists and food analysts.

Revue des Medicaments Nouveaux et de quelque médications nouvelles. Par C. Crinon. 18e Edition. Paris: Vigot Frères, Editeurs, 23, Place de l'Ecole-de-Medicine. 1911.

Among the new substances considered in the eighteenth edition of this work the following may be mentioned: Trichloracetylsalicylic acid, acoine, antodyne, asurol, bromhydrate of codeine, digistrophane, eulatine, hexamethylenetetramine-guiacol, pantopon, seiffenol, 606, tasi, thilavene and zincopyrine.

Lectures on Cosmetic Treatment. A manual for practitioners. By Dr. Edmund Saalfeld. Translated by I. F. Halls Dally, M.D., with an introduction and notes by P. S. Abraham, M.D. Paul B. Hoeber, 69 East 59th St., New York.

This work has been written apparently with the view that cosmetic treatment is for the regular practitioner and not for the so-called "beauty specialist." Professor Josef has well said: "The

subject of cosmetics has been too long neglected by the medical profession, and on this account has, unfortunately, passed into the hands of unqualified persons." It is probably true that a great many patients who could and should be treated by the general practitioner, if he only knew how, drift away from him and waste their time and money on various advertised nostrums or on other quackery. Dr. Saalfeld's book is written on strictly professional lines, and the work will no doubt prove useful to the general practitioner as well as to the dermatologist.

Some Common Remedies and Their Use in Practice. By Dr. Eustace Smith. Paul B. Hoeber, 69 East 59th St., New York.

Among the subjects treated in this volume are the following: On an Unjustly Neglected Remedy—Tartarated Antimony (tartar emetic); On the Internal Use of the Oil of Turpentine; On the Use and Misuse of Iron Remedies; On the Use of Alkalies in Practical Medicine; On Antispasmodics and the Cure of Spasm; On Some Uses of Opium; On the Use of Sodium Salicylate in Certain Serous Inflammations. The chapters making up this book are reprints of articles contributed to *The British Medical Journal* at intervals during the years 1908 and 1909. Their greatest interest lies in the fact that the author records his experience in using some of the standard medicines. Nearly every practitioner of experience could write a book of a similar character, and the young practitioner is the one who would be most benefited by a perusal of this work.

Compte Rendu du Xme Congrès International de Pharmacie. Tenu à Brusselles du 1er an 6 Septembre 1910. Par Dr. A. Schamelhout. Brusselles: Imprimerie-Lithographie L. Vogels, Rue Verte, 48–50. 1911.

This volume contains an official account of the proceedings of the Tenth International Congress of Pharmacy held at Brussels during the first week of September last year. The papers which were read and the communications which were presented are printed in full. The discussions in connection with the various papers and reports are given in abstract and show careful editing upon the part of Dr. Schamelhout, the secretary-general of the Congress. An interesting account is given of the various excursions, fêtes and receptions that were held. In addition to the list of names of members of the Congress we find a number of photographs of those

prominent in the work of the Congress, as of the two Presidents, Dr. Albert Derneville and Dr. Olivier Kusnick; the Secretary-general, Dr. Albert Schamelhout; and the members of the Committee on Organization.

While the reports that have been published, particularly in the foreign journals (see also this JOURNAL, 1911, p. 24), show that the work of the Tenth International Congress of Pharmacy was eminently successful, it is still more apparent from the Proceedings at hand that a broad fraternal and international spirit dominated the entire meeting, and we feel sure that much good must redound to professional pharmacists throughout the world. The pharmacists of our country are encountering the same difficulties and are attempting to solve the same problems as those of other countries. In each country some progress is being made and it is quite possible for the pharmacists of one country to profit by the experiences of those in other lands, and thus eventually the best practice will be the universal practice. It is certain that we in the United States can profit much by the careful perusal of the deliberations of this Congress and, if we endeavor to catch the stimulating influence of the master minds who contributed to this session at Brussels, our professional and commercial work must be of a higher and more efficient character.

WALLACE PROCTER, PH.M. (1851–1911).

Wallace Procter, Ph.M., was born April 1, 1851, in Philadelphia, at the southwest corner of Ninth and Lombard Streets. He was the only son of William Procter, Jr., and Margaretta, his wife, whose maiden name was Bullock. (She was the first cousin of Charles Bullock, for many years the President of the Philadelphia College of Pharmacy.) Prof. William Procter had a daughter, Mary Goldsmith Procter, who married Samuel S. Green, and is now living at Barto, Florida.

Wallace was sent to private schools by his father for his early education. He then went to the Friends' Central School and graduated at the head of his class. He entered his father's store in 1868, and the next year matriculated at the College of Pharmacy. He successfully passed the examinations in the Junior course, and the following year he did not re-enter college, but acquired a practical knowledge of the drug business in the store. In October, 1871, he

entered the Senior course and graduated in 1872, winning the Alumni Gold Medal. "Magnolia Tripetala" was the subject of his thesis.

After graduation he assisted his father in the drug business, and on the death of his father on February 10, 1874, he entered into copartnership with David Preston, Ph.G. (1865), the firm's name being Wm. Procter, Jr., Co. This partnership continued till October, 1890, when Wallace Procter purchased from Lancaster Thomas the drug business at 1900 Pine Street. Here he remained in active practice for twelve years. On December 17, 1906, he entered the service of the Ohio Valley Drug Company, at Wheeling, West Virginia. He was given full charge of the laboratory and manufacturing department and he remained in this position until the day of his death, which occurred on May 27, 1911.

Wallace Procter was a devoted and earnest worker for his Alma Mater. He was elected a member of the Board of Trustees in 1883; and in 1888 he became a member of the Committee on Examinations, and its Chairman in 1890. His keen mind and comprehensive knowledge of pharmacy especially adapted him for this position. The questions which he propounded were always practical and thoroughly adapted to ascertaining the accuracy and extent of the knowledge of the student. He was no mere copier of old or revamped questions. He had but one thought in his mind, to develop the thinking qualities and reasoning powers of the student, and he attached very little value to mere memorizing. He served seventeen years in this capacity.

He was elected a member of the Committee on Instruction, and also of the Committee on Property; and in 1894 he became a member of the Publication Committee of the AMERICAN JOURNAL OF PHARMACY. In 1893 he was appointed a member of the Committee on Pharmaceutical Meetings of the College.

He was an active member of the Alumni Association; served as its Recording Secretary from 1876–1878, and was a member of the Executive Board for nine years. He was twice elected First Vice-President, 1878 and 1885, and became President of the Alumni Association in 1886. In 1887 he was re-elected member of the Executive Board, and continued in this capacity a number of years. Wallace Procter was one of the pioneer workers in this association, in the early days when this meant devoted and continued service under discouraging circumstances. He lived to see the association flourish and grow, and he was foremost in encouraging college spirit.

He became a member of the American Pharmaceutical Association in 1874, and a member of the Pennsylvania Pharmaceutical Association in 1881. He contributed many papers to the various pharmaceutical organizations and journals. Like his father he accepted service in many capacities where the sole reward was the simple satisfaction of doing good and advancing the interests of pharmacy.

Wallace Procter married Susan Ridgeway Shreve, of Mount Holly, New Jersey. It will be remembered that Mount Holly was the summer home of Prof. William Procter, and Wallace greatly enjoyed the freedom of a life in the open air, amid congenial surroundings of fruit trees, grape vines, and the sights and sounds of rural life. It was here that he met the maiden who was to become his wife, and who still survives him.

Three daughters remain to cheer their mother—Edith Harrison, Marian Grigg, and Margaretta Lippincott.

This simple record of the life work of Wallace Procter gives but a faint idea of his achievements. He possessed an excellent mind, developed by education and environment. In the latter years of his life he gave much time to books. He was an omnivorous reader, and all branches of pharmacy claimed his attention.

His admiration for his father and the great mission which the latter fulfilled were ever before him; and, while he did not inherit the love for original investigation which dominated Prof. Procter's personality, Wallace had an analytical mind and never trusted to surface indications. The son practised what the father taught, and added knowledge fitted for his time and generation.

When he transferred his activities from Philadelphia to Wheeling, his quiet unobtrusive manner and his genial qualities soon endeared him to a host of friends. Further acquaintance added to his popularity, and the Ohio Valley Drug Company sent Wallace Procter to the State association meetings as their representative, and he became one of the most valued members of the Virginia Pharmaceutical Association.

On May 9, 1911, he suffered a stroke of paralysis. His physicians, realizing that his condition was serious, recommended a return to his native city; and upon the arrival of his wife, the sad journey from the hospital, at Wheeling, to Philadelphia was accomplished; and though under distressing circumstances, it was cheered by the reflection that his friends turned out en masse at the home and in the railroad station, and did everything in their

power to testify to the devoted wife the honor and the affection which Virginians always exhibit to those whom they love and trust.

Wallace Procter died on May 27, 1911, and the Board of Trustees, and his college friends in Philadelphia, were present at the last sad rites. He was laid to rest beside his father in Mount Holly, the beautiful place which had witnessed more days of real happiness to both than any other spot on earth.

J. P. R.

THE PHILADELPHIA COLLEGE OF PHARMACY.

QUARTERLY MEETING.

The quarterly meeting of the members of the College was held June 26th at 4 P. M., in the Library. The President, Howard B. French, presiding. Fifteen members were present. The minutes of the Annual Meeting held March 27th were read and approved. The minutes of the Board of Trustees for the meetings held March 7th, April 4th and 11th, May 2d and 16th, were read by the Registrar, and approved. The Report of the Committee on Membership was read by Prof. C. B. Lowe, Chairman. Some statistical information is given in the report and mention made of a number of members who are in arrears for non-payment of annual dues. The members are urged to interest those deemed worthy of membership to have them unite with the College.

The Report of the Committee on Necrology was read by Prof. Henry Kraemer. Since the last report three members have died. Caleb R. Keeney died February 1st, 1911—a graduate of the class of 1846. He joined the College in 1852. He was the oldest graduate and at the same time one of the oldest members.

Thomas M. Newbold, died April 2d, 1911. Joined the College in 1871.

Wallace Procter, died May 27th, 1911. Joined the College in 1874. He was the son of the late Professor William Procter.

The College has lost through the death one of our Honorary Members, Professor Attfield (see this JOURNAL, p. 358).

Another name worthy of mention, although not a member of the College, was one of its most distinguished graduates, Professor Carl S. N. Hallberg.

The Historical Committee, through its Chairman, George M. Beringer, reported that they had not been unmindful of their duties,

but as most of the members of the Committee were also members of the College Committee on the revision of the United States Pharmacopœia that much of their time of late has been occupied with that work.

The Committee on By-Laws, to whom was referred the suggestion to change the time of holding the Pharmaceutical Meetings, reported an amendment to Article XI, Section 1. Action upon which lies over till the next meeting of the College.

The Report of Delegates to the 34th Annual Meeting of the Pennsylvania Pharmaceutical Association held at Bedford Springs, June 20th to 23d, was presented by Professor Lowe. Among the valuable reports were those on "Adulterations" and "Trade Interests," both of which were quite full and of great interest. The report of the Committee on Legislation, by its Chairman, John C. Wallace, aroused much interest. The Pharmacy Bill as amended was referred back to the Committee on Legislation with instructions to prepare a bill and submit to the members one month prior to the next Annual Meeting. Some 30 papers were presented by the Committee on Papers and Queries. The prize of $20 for the best paper read at the previous meeting was awarded to Mrs. C. H. La Wall.

Mr. J. L. Lemberger was elected President. Of the nine appointed delegates, six were present. So many of the graduates of the College were in attendance that the meeting almost looked like an Alumni reunion.

The next meeting of the Association will be held at Buena Vista.

The report of Delegates to the New Jersey Pharmaceutical Association was read by Mr. George M. Beringer, Chairman.

The Annual Meeting was held at Asbury Park, N. J., June 13–16. There was an address of welcome by the Mayor of the city. A proper recognition of "Flag Day" was shown by draping the presiding officer's desk with Old Glory, and the entire Association joining in singing the "Star Spangled Banner." Four of the delegates from the College attended the Meeting and were cordially welcomed. The meeting this year was notable for increased attendance and interest in the proceedings. The papers were more numerous and varied. Professor Kraemer contributed a very interesting paper on the Pharmacognosy and History of the Echinacea. The other papers presented and discussed were on Standard Surgical Dressing, by Mr. F. B. Kilmer; Review of the German

Pharmacopœia, by George M. Beringer, Ph.M.; Window Dressing by Mr. Holzhauer; Neutral Suspension of Salvarsan, by Mr. George M. Beringer, Jr.; Official Pepsin Preparations and Official Iron Preparations, by P. E. Hommel; Calx. U. S. P., by Prof. Chas. H. La Wall. The greatest interest was manifested in the discussion of a proposed new Pharmacy Act for the State. A draft of a proposed bill was presented in printed form as a basis for the discussion. The Association expressed itself as to the principles to be included in a new Pharmacy Act to be presented to the next session of the Legislature. This included a "prerequisite" clause as a leading feature. On the whole the meeting this year was considered a very successful one and fraught with possibilities for many pharmaceutical advances.

The President made the following appointments:

Delegates to the American Pharmaceutical Association Meeting to be held in Boston, August 14–18; Joseph P. Remington, Henry Kraemer, C. B. Lowe, A. W. Miller, George M. Beringer.

Historical Committee: George M. Beringer, Jacob M. Baer, Henry Kraemer, Warren H. Poley, C. A. Weidemann.

Committee on Necrology: Henry Kraemer, E. M. Boring, C. A. Weidemann.

Committee on Nominations: William L. Cliffe, Charles H. La Wall, James C. Perry, Theodore Campbell, George B. Weidemann.

Professor Kraemer proposed the names of two gentlemen for Honorary Membership. According to the rules action is deferred till the next meeting of the College.

Professor Kraemer referred to the death of Wallace Procter, who was for many years a member of the College and of the Board of Trustees, and moved that a committee of three be appointed to draft suitable resolutions to his memory, which being agreed to, the President appointed as members of the Committee: Joseph P. Remington, Joseph W. England and C. A. Weidemann.

ABSTRACTS FROM MINUTES OF THE BOARD OF TRUSTEES.

March 7th. Sixteen members present. Committee on Library reported 1350 accessions (old and new books) from October 26th to February 1st. Many of the cases had been cleaned. 132 persons had used the Library during the month. Committee on Examina-

tions reported that Edward C. Denzler had successfully passed the examination for the Certificate of Proficiency in Chemistry, and was awarded the Certificate.

Committee on Announcement asked that they be authorized to issue a hand-book of condensed information for the use of prospective students. Such a book had been prepared and the Committee was given the power to issue two thousand copies.

The merger of the "Alumni Report" with the "Bulletin" had been very favorably received, and it was believed the change would prove a beneficial one.

April 4th. Fourteen members were present. J. L. Lemberger presiding. A communication from the Secretary of the College was read reporting the names of the officers of the College and three members of the Board elected at the Annual Meeting of the College, held March 27th, 1911. Upon organization of the Board, Mr. George M. Beringer was re-elected Chairman, and Walter A. Rumsey, Vice-Chairman, for the ensuing year. Jacob S. Beetem was re-elected Registrar. The standing committee for the ensuing year were announced by the Chairman. Committee on Library reported 286 accessions; 325 persons had used the Library during the month.

April 11th. Sixteen members present. Committee on Instruction presented a lengthy report covering the work of all the departments of the College in detail and making a number of recommendations, which were acted upon separately and adopted with slight alterations in several of them. The Committee on Appropriations reported the various estimated amounts to be allowed the Committees and Departments authorized to make expenditures.

May 2d. Sixteen members present. Committee on Library reported 313 books stamped, classified and shelf-listed, and that 192 persons had used the Library during the month.

Committee on Examinations reported Charles Duvoisin as having passed the examination for Certificate of Proficiency in Chemistry and therefore entitled to the certificate, which was awarded him.

May 15th. George M. Beringer, Jr., was elected to active membership. Seventeen members present. Committee on Examinations reported the names entitled to the degree of Doctor in Pharmacy, Pharmaceutical Chemist, and Certificate of Proficiency in Chemistry and Pure Food and Drug Course, and recommended their election. A ballot being taken they were declared elected.

The award of prizes to those entitled to them was announced, as also the various speakers who were to present the prizes to the recipients on the night of the Commencement.

Committee on Commencement reported that Prof. Willis L. Moore, Chief of the Weather Bureau, had kindly consented to deliver the annual address.

C. A. Weidemann, M.D.,
Recording Secretary.

CORRESPONDENCE.

BOARD OF TRUSTEES, UNITED STATES PHARMACOPŒIAL CONVENTION.

The General Medical Convention edited and published the first Pharmacopœia in the series of what is now known as the Pharmacopœia of the United States of America. It was published in Boston, December 15, 1820. The convention provided for the revision of the Pharmacopœia in 1830, the convention being then known as the National Medical Convention. The same name was applied to the conventions of 1840 and 1850. In 1860 the name was changed to the National Convention for Revision of the Pharmacopœia. In 1900 the name was again changed to the United States Pharmacopœial Convention, which was duly incorporated. Prior to 1900 business matters, as well as the work of editing, were taken care of by the Committee of Revision. With the incorporation in 1900, business affairs were separated from the work of revision and placed in the hands of a Board of Trustees, having the management of affairs and funds of the convention. The By-laws provide that the Board of Trustees shall transact business involving financial or other matters that may be for the best interests of the convention, and perform such other duties as the convention may from time to time direct. The following is the Board of Trustees, as constituted by the convention of May, 1910:

James H. Beal (Chairman), Henry M. Whelpley (Secretary), Frederick W. Meissner, Jr., William Jay Schieffelin and George H. Simmons. Joseph P. Remington and Harvey W. Wiley are ex-officio members. The officers were re-elected for the ensuing year.

The Board held its first annual meeting for the decennial period, 1910–20, at Philadelphia, May 5 and 6. All members were present.

The Board appropriated funds for use in paying necessary expenses in the work of revision incurred by members of Executive Committee under the direction of Chairman Remington.

The Board decided to withdraw from sale those copies of the U.S.P. VIII in which additions and corrections have not been incorporated in the text.

An inventory has been prepared of all of the articles of permanent value purchased since 1900. A record is being made of the location and condition of these articles.

Insurance has been taken out on the electroplates for both the Spanish and English editions which are in the hands of the publisher. Also, on the copies of both the English and Spanish editions which are on sale in the hands of agents.

An auditing committee examined the accounts of the Treasurer, Samuel L. Hilton, and Secretary of the Board, H. M. Whelpley, and found the same correct. Expenditures are first authorized by the Board and the bills approved by the person under whose supervision the expense is incurred. All bills are next sent to the Secretary of the Board to be audited. The Secretary then issues a voucher check which he signs and forwards to Chairman Beal, who in turn signs and forwards the voucher check to Treasurer Hilton, who signs same and mails it to the payee. The original bills with notations are preserved with the records of the Secretary of the Board. The Treasurer of the Convention and the Secretary of the Board keep duplicate accounts of receipts and expenditures, as shown by the voucher checks. The following is a summary of the same for the fiscal year just closed (May 1, 1910, to April 30, 1911):

RECEIPTS.

May 23, 1910, To balance from Treasurer 1900–1910....	$8394.01
May 23 to April 30, 1911, Sales English Edition........	6188.02
May 23 to April 30, 1911, Sales Spanish Edition........	1169.35
May 23 to April 30, 1911, Receipts from Use of Text....	290.00
July 1, 1910, Interest on Deposits, American S. & T. Co..	88.91
January 3, 1911, Interest on Deposits, American S. & T. Co.	83.02
Total Receipts	$16,213.31

EXPENDITURES.

1910–11. Expenses 1910 Convention.—Supplies, $79.70; printing, $53.25; general, $15.73; stenographic report, $375.38; clerical, $198; abstract, $345.17; total, $1067.23.

I. Revision.—Clerical, $1847.50; meetings, $13.89; supplies,

$1140.97; postage and telegraph, $146.88; experts, $52.60; general, $112.67; total, $3314.51.

II. Publication and Sales.—English edition, $1952.56; Spanish edition, $271.12; general, $9. Total, $2232.68.

III. Administration.—Meetings, $330.10; clerical, $666; supplies, $154.65; postage and telegraph, $67.50; general, $41.53. Total, $1259.78. Grand total, $7874.20.

Cash on deposit American Security Co., to balance, as shown by Treasurer Hilton's books and verified by the bank, $8339.11.

HENRY M. WHELPLEY,
Secretary Board of Trustees, U.S.P.C.

KENTUCKY AGRICULTURAL EXPERIMENT STATION.

To the Kentucky Retail, Wholesale and Manufacturing Druggists:

Two years' work under the Kentucky Food and Drugs Act has convinced those engaged in the enforcement of the drug sections of that Act, that there are two classes of adulteration: first, adulterations due to wilful intent or gross carelessness; second, adulterations due to various tráde and professional problems, which this office believes can be better overcome through mutual assistance rather than prosecution.

For the purpose of introducing educational and co-operative methods with respect to the second class problems, this Division proposes to conduct a short term school for druggists and others engaged in the drug business, of about ten days' duration, during the last of April or the first of May. It is proposed to take up at this school the following subjects: (*a*) The general application of the State and Federal pure food laws for the drug business; (*b*) the drug regulations and notices of judgment under the Federal law; (*c*) the regulations under the State law; (*d*) the proper labelling of patent and proprietary medicines under the law; (*e*) the proper labelling of U.S.P. and National Formulary products under the law; (*f*) necessary equipment for a druggist's laboratory; (*g*) drug store management and equipment; (*h*) problems connected with the preparation, storage and handling of various pharmaceutical preparations; (*i*) standard weights and measures; (*j*) the soda fountain; (*k*) other similar subjects.

These matters will be presented by the experts of this office

and by pharmacists who will be invited to assist. The Division also proposes to invite the manufacturers of some of the pharmaceuticals with which druggists have difficulty, to send their chemists or manufacturing managers to give special lectures with respect to the proper treatment and handling of such products.

This office would like to have your views of the school, and the plan outlined above, with any further suggestions, as to whether or not anyone connected with your firm will attend, and as to the best date.

A blank for reply is enclosed herewith. Please answer at your earliest convenience. Respectfully,

R. M. ALLEN,
Head of Division.

March 22, 1911.

AMERICAN JOURNAL OF PHARMACY,
Philadelphia, Pa.

GENTLEMEN: Enclosed find three resolutions adopted at the last meeting of the Pennsylvania Pharmaceutical Association.

The one regarding the Pure Food and Drugs Act and also the one concerning Dr. Wiley are particularly pertinent at the present time, in view of the activity of the food and drug "Dopers."

These resolutions have been sent to the President of the United States, the Senators from Pennsylvania, and the Congressmen from the State of Pennsylvania.

Thanking you for your uniform courtesy and assistance,

Very sincerely yours,

E. F. HEFFNER,
Secretary.

July 21, 1911.

Resolution: We, the members of the Pennsylvania Pharmaceutical Association, in convention assembled, do hereby

Resolve, That we place ourselves on record as favoring such necessary amendments to the Federal Food and Drugs Act of June 30, 1906, as will prevent the misbranding of food and drug products either as to composition, curative action or in any other particular.

Resolution: We, the members of the Pennsylvania Pharmaceutical Association, in convention assembled, do hereby

Resolve, That we disapprove of and denounce the underhanded and unfair methods which have recently been used by the organization called the American Protective Association in attacking Dr.

Wiley, who has so fearlessly fought for honest standards in both foods and drugs; for, while many persons may honestly object to certain rulings and proceedings brought under the Federal Food and Drugs Act, we believe that such objections as are meritorious and such opposition as is worthy of support should be brought in an open and fearless manner and without subterfuge.

Resolution: Whereas, there is pending in Congress an act known as "The Sherley Bill," H.R. No. 8,887, under the provisions of which it is proposed to levy a stamp tax of 2½ per cent. based upon the retail price of so-called "patent" or "proprietary" medicines and all toilet preparations of a proprietary character, and

WHEREAS, Experience has demonstrated that this burden will fall heavily upon the retail druggist because the added cost cannot be passed to the consumer as the retail price is fixed by the manufacturer, and

WHEREAS, The only medicines that are really patented, viz., the various imported and domestic synthetic products will not come under the provisions of this act, for reason that they are classified as uncompounded medicines upon which this tax would not be levied; therefore be it

Resolved, That we, the members of the Pennsylvania Pharmaceutical Association, in convention assembled, do solemnly protest against the enactment of this measure, believing it to be a direct tax upon a single class of business, and therefore burdensome and unjust.

PENNSYLVANIA PHARMACEUTICAL EXAMINING BOARD.

LICENSED AS PHARMACISTS.

Announcement was made by the State Pharmaceutical Examining Board on July 6th that 334 out of 450 applicants for State licenses had been successful, the number qualifying as pharmacists being 199 and as assistants 135.

Philadelphians who passed the examinations are:

Pharmacists: Samuel Baradofsky, William D. Baun, Jennie Bellitz, Louis Bell, Meyer Bloomfield, Frank E. Houston, De Wilton S. Berry, Samuel J. Brahin, Osher Briskin, Robert O. Bricker, Lloyd Burtt, Franklin C. Brush, Louis E. Christopher, Philip Cohen, D. Wayne Darrah, Charles C. Eberly, David W. Eisman, Lewis Fleisher, Nathan M. Friedman, Walter J. Gaskill, Samuel Glick,

Jacob Goldberg, Charles S. Gutzeit, Morris Haimowitz, Gerald J. Harrigan, Max Heller, Carl F. Kaehler, Nathan Kaufman, John L. Kooker, Jr., James Kramer, John F. Kratz, Harry Lashinsky, Rebecca Levy, Andrew F. Lippi, Michael J. Lovenstein, Francesco Megaro, Samuel Millrood, Louis H. Myers, Mabel Nelson, Lewis W. Oswald, A. A. O'Daniel, John M. O'Donnell, Geo. W. Patterson, Jr., Benjamin Promisloff, John W. L. Purcell, Albert Rachmil, Julius Rapaport, Nathan Rosensweet, Samuel Rosin, Leon Ross, Thomas B. Tanner, Isador P. Salinsky, Fred A. Schuenemann, Edward Seldes, Nathaniel J. Segal, Stanley A. Shiles, Samuel A. Silk, M.D., Israel Spiers, Ethelbert Steelman, Morris Stein, William H. Sternthal, William H. Udell, Lewis Viner, Llewellyn J. Watkins, E. Leonard Weiszgerber, Leon M. Wolchek, Harry Woorman, Jos. L. Murray.

Qualified Assistants: Gerson Azoff, Rose Blieden, Maurice Brown, Herman J. Broude, Charles A. Buohl, Herbert H. Boyer, Ernest Bernabei, F. W. Campbell, Joseph Duffy, James T. Fiedler, Harry Friedman, M. S. Glauser, Herman Leo Hinski, Ralph A. Hurley, William F. Kalesse, Karl Krogh, Albert F. Keller, Morris I. Lopoten, Jacob Lubin, Moses Minzes, Myer Matrick, Patrick P. Maloy, Fred W. Martin, Leah Nichols, Esther Nicholas, H. E. Newton, Blair G. Rumsey, L. E. Rothberg, C. J. Rabin, Clifford Raser, Henry L. Reinish, Hyman B. Stern, M.D., Sol. E. Streitfeld, C. B. Sterner, J. Harry Swain, Edison Shoemaker, Henry A. Stauffenberg, Tany Taboror, Anna Teller, B. O. Tegge, John Thomas, Antonio Venuto, David Weinberg, Hirsh Wilderman, W. S. Wignall, Reuben L. Walton, O. W. Wickham, Charles H. Yeagle, and Nathan Zonies.

The colleges of pharmacy and the number of applicants from each who graduated in 1911 and took the examinations for applicants desiring registration as pharmacists, were as follows:

Philadelphia College of Pharmacy, 70, of which 66 passed the examination and 4 failed; Medico-Chirurgical College, department of pharmacy, 34, of which 28 passed and 6 failed; University of Pittsburg, department of pharmacy, 44, of which 42 passed and 2 failed; Temple College, department of pharmacy, 15, of which 14 passed and 1 failed; Brooklyn College of Pharmacy, 1 applicant and 1 successful.

The next examinations given by the board will be conducted in the Williamsport High School, Williamsport, Pa., on August 24 and 25.

THE AMERICAN

JOURNAL OF PHARMACY

SEPTEMBER, 1911

THE PHARMACOPŒIAL STANDARD FOR DESICCATED THYROID GLANDS.[1]

By Reid Hunt and Atherton Seidell,

[Division of Pharmacology, Hygienic Laboratory, U. S. P. H. and M. H. Service, Washington, D. C.]

During the past few years a great many experiments have been made in this laboratory upon the relation between the physiological activity of thyroid and its iodine content. These experiments, and practically all others that have been described in the literature, demonstrate this parallelism; it may therefore be concluded that at present the most satisfactory way to standardize thyroid is by means of the determination of the organically combined iodine which it contains. From the standpoint of the Pharmacopœia the question resolves itself simply into the selection of the most satisfactory method for the iodine estimation and the adoption of the most reasonable percentage content of iodine as the standard.

Of the methods which may be used for the determination of the iodine there are only two which need to be considered, viz., the older Baumann method which consists of fusion with caustic alkali, liberating the iodine by suitable means from the aqueous solution of the fused residue, extracting it with an immiscible solvent, and estimating its quantity colorimetrically, and the recently proposed Hunter method, which differs from the above in substituting alkali carbonates for the fusion, conversion of the iodine to the iodic state, and estimating its amount by a volumetric procedure. Of these two methods the latter has been found by us to possess advantages both in reliability of the results, and

[1] Read at the Boston Meeting of the American Pharmaceutical Association, August, 1911.

convenience of execution. Furthermore, from the point of view of the Pharmacopœia it possesses the advantage over the Baumann method that no analytical procedures, volumetric solutions, or reagents, new to the present edition of the Pharmacopœia, are required.

In his original paper[1] Dr. Hunter gives very clear and explicit descriptions of all the details of the process, and there is consequently little opportunity for uncertainty in regard to any part of the method. It is the rule, however, in Pharmacopœial descriptions of analytical processes, that only the essential features be included, consequently it appears desirable that a concise description of the Hunter method, in what may be called Pharmacopœial language, be given. Such an outline would be as follows:

Determination of Iodine (Hunter Method).—One gram of Desiccated Thyroid Gland is mixed in a nickel crucible of about 125 c.c. capacity, with 15 grams of a mixture composed of 138 parts by weight of anhydrous K_2CO_3, 106 parts anhydrous Na_2CO_3 and 75 parts KNO_3, and an additional 5 grams of this fusion mixture spread evenly over the surface. The crucible is then heated over a free Bunsen flame until no further carbonization is observed, it is cooled and the friable residue dissolved in about 150 c.c. of distilled H_2O. To this solution contained in an Erlenmeyer flask of about 500 c.c. capacity, is added approximately 50 c.c., or its equivalent, of fresh liquor sodæ chlorinatæ U. S. P. (containing 2.4 wt. per cent. Cl). The mixture is then treated with enough phosphoric acid (1 volume of the 85 per cent. syrup and 1 volume of H_2O), to produce a marked yellow tint of free chlorine, and an additional 10 c.c. of the phosphoric acid is then added and the contents of the flask boiled for about one-half hour or until the volume has been reduced to about 150 c.c. The liquid is cooled, 10 c.c. of 1 per cent. aqueous KI solution is added and the liberated iodine titrated with N/200 sodium thiosulphate, adding starch paste as the indicator just before the end of the reaction. The N/200 thiosulphate may be made by diluting 25 c.c. of exactly N/10 thiosulphate to 500 c.c.; it changes strength rapidly and should be prepared fresh at each time determinations are made. One c.c. of N/200 thiosulphate corresponds to 0.0001058 gm. iodine derived from the sample of thyroid used.

This method has been tested in this laboratory in comparison

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[1] Hunter: Jour. Biol. Chem., 7, 321–349, 1910.

with the Baumann method, upon quite a large number of samples of commercial desiccated thyroid glands. The agreements in duplicate determination by the Hunter method were found to be considerably more uniform than those by the Baumann method, and the results in practically every case were from 10 to 15 per cent. higher. Since there is a reasonable source of loss at one step of the Baumann method, viz., the acidification of the aqueous solution of the fusion residue, and this particular cause of loss has been obviated by Hunter in his method, there can be little doubt that the higher results are the nearer correct.

Of the commercial samples which we have so far examined, some were purchased on the market during 1907, and the others recently received direct from two American firms which prepare thyroid glands for medicinal use. For these latter we herewith acknowledge our indebtedness to Armour and Co., and Parke, Davis and Co. The samples received direct are portions of the several lots prepared at the particular dates shown in the table.

Percentage of Iodine in Commercial Desiccated Thyroid U. S. P. as Determined by the Hunter Method.

Laboratory No.	Source.	Per cent. I.	Laboratory No.	Source.	Per cent. I.
99	P. D. & Co. (1907)	0.185	104	Armour & Co. (1907)	0.138
99(a)	P. D. & Co. (1907)	0.185	107	Armour & Co. (1907)	0.145
100	P. D. & Co. (1907)	0.188	108	Armour & Co. (1907)	0.138
101	P. D. & Co. (1907)	0.153	109	Armour & Co. (1907)	0.141
102	P. D. & Co. (1907)	0.162	109(a)	Armour & Co. (1907)	0.142
103	P. D. & Co. (1907)	0.219	119	Armour & Co. (1907)	0.135
105	P. D. & Co. (1907)	0.138	120	Armour & Co. (1907)	0.129
106	P. D. & Co. (1907)	0.218	121	Armour & Co. (1907)	0.140
106(b)	P. D. & Co. (1907)	0.212			
116	P. D. & Co. (1907)	0.118		Average	0.138
117	P. D. & Co. (1907)	0.117	345	Armour & Co. Dec. 16, '09	0.279
118	P. D. & Co. (1907)	0.158	346	Armour & Co. Jan. 23, '10	0.095
	Average	0.171	347	Armour & Co. Feb. 15, '10	0.212
			348	Armour & Co. April, '10	0.162
358	P. D. & Co. (1911)	0.206	349	Armour & Co. May, '10	0.146
359	P. D. & Co. (1911)	0.206	350	Armour & Co. June, '10	0.271
360	P. D. & Co. (1911)	0.154	351	Armour & Co. July, '10	0.202
361	P. D. & Co. (1911)	0.214	352	Armour & Co. August, '10	0.231
	Average	0.195	353	Armour & Co. Sept., '10	0.215
			354	Armour & Co. October, '10	0.144
			355	Armour & Co. Nov., '10	0.252
			356	Armour & Co. Jan. 16, '11	0.219
				Average	0.202
			357	Thyroid Proteid (Armour)	0.607

From the above results it is found that the average of the 12 P. D. & Co. samples received in 1907 is 0.171 per cent. I, while that for the Armour samples is 0.138 per cent. On the other hand the average per cents. for the recent samples are respectively 0.195 and 0.202, thus showing that in both cases products with higher iodine contents are being prepared. On the whole these results show a very commendable degree of regularity in the percentage of iodine in thyroid at present on the market. With very few exceptions none of these samples might be expected to produce a noticeable variation in physiological effect. There can be no doubt, however, that the interests of both the producer and consumer would be safeguarded by the establishment of a reasonable Pharmacopœial standard of iodine content. Judging from the results upon the samples supplied by the manufacturers themselves, such a limit could be fixed at approximately 0.2 per cent. I. without causing an undue hardship. This per cent. has already been adopted by an English firm. Of course sufficient latitude, of say 0.03 per cent. above or below this figure, should be permitted, thus making the extreme limits 0.17 to 0.23 per cent. iodine.

The remaining Pharmacopœial description which is necessary is that limiting the source of the raw material to certain animals and prescribing a reasonable limit of moisture and ash, which from our experiments might be placed at not exceeding 6 per cent. for the former and 5 per cent. for the latter, and finally the prohibition of all iodine in inorganic or any other form of combination than that peculiar to the thyroid.

In regard to the ash content it should be mentioned that in general those samples with the higher percentage of iodine contain the lower percentage of ash, and vice versa. Thus for instance, of 12 samples containing more than 0.2 per cent. iodine the variation in the ash content was from only 3 to 4 per cent., while 6 samples containing approximately 0.15 per cent. iodine contained more than 4 per cent. ash, and one sample with only 0.095 per cent. iodine contained more than 5 per cent. of ash.

It has recently been suggested by certain investigators that the iodine of thyroid may not all be present in an equally physiologically active form, and consequently that it was possible by certain manipulative processes to remove the less active forms and retain the more active portion in a product which is therefore supposed to contain iodine in a super active condition as compared with that

of the untreated material. A number of experiments which we have recently made with one of these products, designated as Thyroid Proteid, have failed to confirm this hypothesis. These recent experiments indicate even more conclusively than our previous work, the constant behavior of the thyroid-iodine substance and the close relation between the iodine content and the physiological activity of both the desiccated thyroids and the new Thyroid Proteid.

COLORIMETRIC TEST FOR CARAMEL.[1]

By F. A. Upsher Smith, Pharmaceutical Chemist.

Within the past year the question of standardizing the color of Caramel has been engaging the attention of pharmaceutical workers.

Dr. George A. Menge recently suggested the preparation of a standard solution of Caramel by boiling on a water bath for five minutes one-half gram of Sugar with 5 c.c. of a mixture of Sulphuric Acid 2 c.c. and water 10 c.c. The resulting mixture, partially cooled by the addition of 25 c.c. cold water, neutralized with Potassium Hydroxide Solution and finally diluted to 100 c.c. forms the standard color with which to compare commercial samples of Caramel.

The standard that I have used for several years seems to me to be one that is more readily applicable, as the materials are always on hand and the method is a simple and quick one. The method consists in matching a given sample of Caramel against a standard color consisting of a Nesslerized solution of Ammonia. For carrying out the test, make a stock solution of Ammonium Oxalate by dissolving .0417 gm. of Monohydrated Ammonium Oxalate, in crystals, in 1 litre of distilled water. Prepare the standard color by taking 10 c.c. of this stock solution, adding 38 c.c. of water and 2 c.c. of Nessler's Solution.

Match the standard color with the Caramel prepared as follows: Dissolve 1 gm. of the Caramel in water and make up to 1 litre. Run the solution from a burette into a Nessler glass until, on dilution with distilled water to 50 c.c., it exactly matches the standard color.

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[1] Read before the annual Convention of the Minnesota State Pharmaceutical Association, Duluth, Minn., July 12, 1911.

As an arbitrary standard, consider the standard Caramel as one of which 0.01 gramme (represented by 10 c.c. of the diluted solution made up to 50 c.c. with water) is required to match 50 c.c. of the color standard. Call this standard Caramel 100 per cent. Caramel as found on the market will usually test around this figure.

To obtain the Colorimetric value of any other Caramel divide 100 x 10 by the number of c.c. of the diluted Caramel Solution required. For example, in a particular test, 20 c.c. of the solution of the sample of Caramel were required to match the color standard. Then the Colorimetric value of the Caramel sample equals $\frac{100 \times 10}{20} =$ 50 per cent. In other words, this particular sample was one-half strength. This strength is a convenient one for making elixirs.

Among the advantages of this method I might mention that the tints of the Ammonia Solution and diluted Caramel Solution are practically identical. The materials for making the test are to be found in every laboratory and the apparatus required consists simply of a burette, pipettes, and two Nessler glasses. The two vials of liquid before you show how similar these solutions are in tint and illustrate the practicability of the method. This method is particularly valuable from the fact that it enables the operator to give a numerical value to any given sample of Caramel, a point of importance in making purchases, as well as in the manufacturing laboratory.

Laboratory of Noyes Bros. & Cutler, Saint Paul, Minn.

THE FIXATION OF SULPHIDE BY BASIC BISMUTH COMPOUNDS.

By J. L. Stingel.

From the Cleveland School of Pharmacy, Cleveland, O.

In a letter to the *J. A. M. A.* (July 16, 1910, Vol. 55, p. 236), Dr. Hulse describes his experience with the so-called creams, milks or magmas of bismuth, in the treatment of infantile disorders, particularly calling attention to the fact that the characteristic brown or black color of the stools was absent.

At the suggestion of Prof. Sollmann, of the Western Reserve University Medical College, the writer made a number of experi-

ments in order to determine if there were any chemical basis for such a difference, in other words, whether the various basic bismuth salts really differ in their behavior toward sulphides.

In the first series of experiments the sulphides were applied directly to suspensions of bismuth salts (0.5 gm. with water q.s. —25 cc.). The reaction of the suspension to litmus paper was noted, through one set of samples a current of H_2S was passed to saturation. To the other Ammonium Sulphide $(NH_4)_2S$ sol (5 cc.) was added.

Suspensions	Reaction	H_2S	$(NH_4)_2S$
Bismuth Magma (dried) old.....	Neutral	Positive	Positive
Bismuth Magma (dried) new....	Neutral	Positive	Positive
Bismuth Subcarbonate	Neutral	Positive	Positive
Bismuth Subgallate.............	Neutral	Positive	Positive
Bismuth Subnitrate	Neutral	Positive	Positive
Bismuth Subsalicylate..........	Neutral	Positive	Positive

Two samples of finished Creams of Bismuth, one made by the N. F. process, the other by Raubenheimer's modification, were tested with $(NH_4)_2S$; both gave dark ash colored ppts.

It will be seen that the sulphide is formed in all, but somewhat less readily in the old magma.

A second series of experiments was made to determine whether any bismuth goes into sol. in water. 0.5 gm. of the Bismuth subsalt in water q.s. 25 c.c. was allowed to stand 24–48 hrs., frequently agitated, filtered and filtrate brought up to 25 cc. These filtrates were tested the same as the first series.

Filtrates	Reaction	H_2S	$(NH_4)_2S$
Bismuth Magma (dried) old.....	Neutral	Negative	Negative
Bismuth Magma (dried) new.....	Neutral	Negative	Negative
Bismuth Subcarbonate..........	Neutral	Negative	Negative
Bismuth Subgallate.............	Neutral	Positive	Positive
Bismuth Subnitrate.............	Neutral	Positive	Positive
Bismuth Subsalicylate..........	Neutral	Negative	Negative

Conclusions.—The suspensions of the various basic bismuth salts are practically, equally effective in binding H_2S but in old magma this property is impaired.

Water left in contact with the basic bismuth salts dissolves some bismuth from the subnitrate and subgallate but none from the others.

STANDARD SURGICAL DRESSINGS.[1]

By Frederick B. Kilmer.

The subject of standardization of surgical dressings was a prolific theme of discussion during a period beginning in 1893. A reference to the journals of that time will disclose the questions then at issue, and need not be here entered into. To understand the present day situation, it will be necessary to review somewhat the history and technic of surgical practice.

A recent writer, Dr. Robert T. Morris, tersely sums up the situation as follows:

"Surgery is now in the dawn of the fourth era. In the days of Hippocrates surgery was heroic. That represents the first era. Then came Vesalius and the anatomists, and we had the second or anatomic era. Pasteur and Lister introduced the third, or the pathologic era. While this third, or pathologic era, is now prevailing to a great extent, it is rapidly passing to what this authority named as the fourth or physiological era."

The dominant idea of this fourth era is to prevent the development of bacteria in wounds, and to remove the products of infection by means of the art. The present day surgical dressing has been evolved out of the Listerian era. Peculiar to the Listerian era, especially in its opening period, was the use of antiseptics, which were applied in the form of sprays, irrigation, washing and the like.

Lister devised a series of dressings made by combining an antiseptic, chiefly carbolic acid, with resins and paraffin, somewhat resembling a cerate or plaster mass; this was poured while hot into meshes of lint, afterwards upon gauze cloth. The intention of this dressing was that the gauze should adhere to the flesh and that the vehicle or cloth should prevent the volatilization of the carbolic acid. Very quickly it was found more convenient to take a piece of gauze or cotton and dip it into antiseptic solutions such as were then in use.

The National Formulary of this period contained a formula for carbolized gauze, essentially an adhesive mass containing carbolic acid. The Formulary at this time adopted as a standard of fabric, a market gauze known as Lehigh E.

It is perhaps interesting to note that the amount and strength

[1] Read at the meeting of the New Jersey Pharmaceutical Association, June 14, 1911.

of the antiseptics used at this time were markedly different from these in use to-day. For example, we find at this time acid used in a strength of 1 in 12, 1 in 20; corrosive sublimate 1–200, and iodoform 20 per cent.

The method of preparing iodoform gauze in the practice of the originators may be mentioned: Iodoform was first used by dusting directly over the wound. Bilroth afterwards stated that when the iodoform was dusted over the fibre of cloth it was less irritating than when applied directly to the wound, and he later adopted a dressing containing 20 per cent. iodoform.

A feature of this period was the English practice of using boracic acid in a strength as high as 40 per cent. It is stated that this was fostered by the producers because the dressings were sold by the pound, and boracic acid was much cheaper than the fabric.

This was only two decades ago. Now we find that carbolic acid, the agent which helped in the revolution of the world of surgery in the time of Lister, has passed into disuse in surgical technic; that the strength of corrosive sublimate, and its preparations, has become weaker and weaker until there is now demanded a strength of 1–10,000; that iodoform has shrunk from a strength of 40 per cent. to 2 per cent.; and that many antiseptics once in very large demand and for which much was claimed have been forgotten.

In the later days of the third era of surgery and in the opening of the fourth era, antiseptic surgical dressings have been but little used. The demand is now for sterilized cotton, sterilized gauze, sterilized bandages. If antiseptics are used they are applied in certain classes of cases and as an adjunct—not as an important part of the technic. The surgeons are learning the value of procedures briefly characterized as "skilful neglect"; they are learning that antiseptics even in a weak solution are damaging to the growth of new tissue; that sterilized water produces untoward results; and that the much lauded hydrogen peroxide is destructive. Some go so far as to claim that cotton or gauze placed ever so gently upon a surface undergoing cell repair is harmful, because new cells are caught in the fibrous mesh and torn away when the dressing is changed.

All that is necessary, is a protection medium. At best in the present day practice we have to consider only plain absorbent gauze cloth in its various forms, such as bandages, tapes, etc., and absorbent cotton. These two substances represent almost entirely the surgical dressing of the period.

In view of the facts cited, and for other reasons which might be urged, it would seem to me to be a useless proceeding for either the Pharmacopœia or the National Formulary to attempt to standardize surgical dressings, especially those of the antiseptic or medicated type.

It will readily be seen that in the period covered by the Eighth Revision of the Pharmacopœia, this type of dressings has radically changed, and for the most part has gone out of existence, and unless the Pharmacopœia and the National Formulary are revised much more rapidly than has been the case in the past, any such standardization would become obsolete soon after its publication. Antiseptic dressings are the relics of a rapidly changing practice—an era of surgery which has passed, and thus for the druggist, belong to a declining trade.

As of some slight interest we may here insert a table prepared sometime ago by one of the manufacturers of surgical dressings, which was intended to show the consumption of surgical dressings made of cotton. It is as follows:

COTTON USED IN SURGERY IN THE UNITED STATES.

	1878	1886	1898	1910
Raw cotton (lb.)	1,000	5,000	20,000	25,000
Absorbent cotton (lb.)	5,000	250,000	3,000,000	5,000,000
Bandages (lb.)	10,000	20,000	100,000	200,000
Gauze (yds.)	1,200	120,000	20,000,000	50,000,000
Lint (lb.)	50,000	45,000	40,000	40,000
Miscellaneous dressings (lb.)	500	2,000	20,000	35,000

While the consumption of antiseptic dressings was not enumerated in the table, it may be stated that in the face of this enormous increase in certain types, antiseptic dressings have steadily and rapidly declined, until some of them have gone out of existence. As an example of these which have almost entirely disappeared we may instance salicylated acid cotton, styptic cotton, iodized cotton, iodoform cotton, Lister's cyanide of mercury and zinc gauze, and salalembroth cotton and gauze.

Various formulas for antiseptic cottons and gauzes may be found in the British Pharmaceutical Codex, the French Codex, and Deitrich's Pharmazeutisches Manuel, and other works to which the

reader is referred. They need not be discussed except briefly to call attention to some of the formulas given in the British Pharmaceutical Codex, where, under the head of Carbolized Cotton, attention is called to the fact that the preparation soon loses strength by exposure; it is only of approximate strength when freshly made.

In certain instances, in capsicum cotton and mercuric iodide cotton, it is recommended that the cotton be dyed in order that it may appear to the eye as of normal strength. In the case of corrosive sublimate cotton the statement is made that this soon deteriorates. In the case of carbolic acid gauze, cyanide gauze, and iodoform gauze—it is noted in the Codex that they undergo rapid change—and in the case of corrosive sublimate it is stated that the mercuric chloride undergoes decomposition in a month or six weeks.

These statements from an official authority would indicate that it would be difficult to formulate an absolute standard to be embodied in a Pharmacopœia, the legal authority by which preparations named therein shall be judged. In other words, a given antiseptic gauze, prepared exactly according to the official formula, would not and could not retain its conformity to the standard, and were the suggestions embodied in a most excellent paper by Geo. M. Beringer, Jr., AMERICAN JOURNAL OF PHARMACY, April, 1911, where formulas for the preparation of antiseptic gauze dressings are given, with the further addition of a process for sterilization by steam, dry heat, etc., adopted, the difficulty would be greatly increased. Mr. Beringer evidently fails to take into account the fact that his process of sterilization when applied to such preparations as iodoform, thymol, carbolic acid, and other volatile substances, would bring about a complete change in the product, so that the finished article is not what it started to be.

In the early days of the Listerian or antiseptic era of surgery, it was a common custom for the surgeon to prepare his own gauze at the operating table or bedside of the patient. This he did by simply dipping the gauze or cotton into a solution of a given strength and apply it direct to the wound, and this practice applies to a certain extent to-day as an emergency practice, except that the strength of the antiseptic solutions has been greatly modified.

It is my judgment that the pharmacist will only be called upon to prepare antiseptic dressings in extreme cases. Even in emergency practice, plain, sterile gauze or cotton is considered adequate.

When we take up the question of plain dressings, such as cotton

or gauze not impregnated with an antiseptic, there is possibly an opportunity for the Pharmacopœia or the National Formulary to establish certain standards.

I have discussed this question at some length (*Journal of the Society of Chemical Industry*, October 31, 1904). Here I have called attention to the fact that the Pharmacopœial standards thus noted were open for criticism.

In respect to the standards of the United States Pharmacopœia, among its faults are the tests for absorbency. Absorbent cotton, even when heavily charged with impurities, will, when pressed in the hand and placed on the surface of water, sink. The Pharmacopœia is very indefinite as to the amount of water to be used. The United States Pharmacopœia has it that, when purified cotton, previously pressed in the hand, is placed on the surface of cold water, it will absorb the water and sink, and the water should not acquire an acid or alkaline reaction.

The test of sinking in water is a test neither of purity nor absorbing power. Soap or glycerine will increase the apparent absorbency.

The following has been suggested by me as a more rational Pharmacopœial standard for purified or absorbent cotton, and these standards are those to which the leading brands now on the market will be found to comply. In other words, they are standards which are attainable, and which will exclude cottons of a low grade or to which foreign substances have been added:

Gossypium Purification.

Purified Cotton.

Suggested Standard.—The hairs of the seed of Gossypium (Fam. Malvaceœ) freed from adhering impurities and deprived of fatty matter.

White, soft, fine filaments, appearing under the microscope as hollow, flattened and twisted bands, spirally striate, and slightly thickened at the edges; inodorous and tasteless; insoluble in ordinary solvents, but soluble in an ammoniacal solution of cupric oxide.

When purified cotton, previously compressed in the hand, is thrown on the surface of cold water, it should readily absorb the latter and sink.

Purified cotton should contain no more than a very small quantity, if any, of visible impurities, and on combustion of five grammes or more should not leave more than 0.2 per cent. of ash.

Ten grammes of purified cotton are saturated with 100 c.c. neutral distilled water, the water pressed out and divided into two portions, each of which is placed in a white porcelain dish. To one portion is added 3 drops phenolphthalein T. S., and to the other portion one drop methyl orange T. S. Neither portion should develop a pink color (absence of acid or alkali).

If 20 grammes be extracted in a narrow percolator with ether until 300 c.c. percolate is secured, the percolate should on evaporation to dryness in a tared beaker leave a residue of not more than 0.5 per cent. of the weight of cotton used (limit of fatty matter). A blank test should be made with an equal quantity of the ether used.

If 20 grammes be extracted in a narrow percolator with alcohol until 200 c.c. percolate is secured, the percolate should not be of a blue or green tint (absence of dyes) and on evaporation to dryness in a tared beaker the residue should amount to not more than 0.5 per cent. of the cotton used (limit of resins and soap). A blank test should be made with an equal quantity of the alcohol used.

If 20 grammes be extracted in a narrow percolator with hot distilled water (80° to 90° C.) until 200 percolate is secured, the percolate should not be clouded (absence of soap), and on evaporation to dryness in a tared beaker the residue should amount to not more than 0.2 per cent. of the weight of cotton used (limit of soluble salts). A blank test should be made with an equal quantity of the water used.

Gauze cloth, otherwise known as surgical gauze, came into use as a wound dressing with Listerism. Lister first applied lint, afterwards what was known as cheese cloth, which by evolution, was converted into surgical gauze, and finally a combination of absorbent gauze and cotton. The tendency of modern surgical technic has been to simplify dressings. All other substances have to a large extent been abandoned and gauze made to constitute almost solely the dressing material.

A good quality gauze has numerous and obvious advantages over any other material for this purpose. It is highly absorbent, pliable, with an open texture that is firm and strong. It is free from the loose fibres and irritating particles found in unspun cotton. It is cool, light, and readily shaped into required forms.

Surgical gauze in the operating room acts primarily as a covering and protective, and if of sufficient thickness filters the external air that passes through to the wound. It is firm enough to bring together any incised or separated parts. Its fibres act, to a certain extent, as plugs or compressors to the small blood-vessels which may have been severed. The absorptive power of good gauze is ample to receive and retain a sufficient quantity of blood to coagulate and coat the injured part and thereby check the flow.

Gauze is also employed to absorb discharges which would infect the surrounding area if not seized upon by an absorbent and removed. In the early technic antiseptics of disinfectants were used to impregnate gauze dressings. In modern surgery a piece of sterile gauze is sometimes the only dressing employed.

Taken altogether surgical gauze may be considered the most convenient and the most useful dressing material now known.

Gauze cloth in the cotton trade is known as "Cheese Cloth," "Tobacco Cloth," or unbleached gauze, and it is quite distinct from surgical gauze, although large quantities of the former are used for surgical purposes. In England and on the Continent gauze is spun and woven solely for surgical uses, and there is one such maker in the United States.

The method of preparing cotton fibre for manufacture into surgical gauze is described in the paper heretofore cited, and consists of a long series of mechanical and chemical processes, a description of which lies outside of our present purpose.

In the surgical gauzes as found on the market there is a marked variation in the length of the fibre, the size and weight of the thread, yardage per pound, and other physical and chemical characteristics. The earlier surgical gauzes were made of Egyptian cotton, carried an equal number of threads each way, and were hand-finished. The hand-finish process kept the thread straight, the final product was less white, but more elastic.

In some samples of gauze in our market there will be found certain dressings or loadings added to improve appearance, to increase the weight, to assist in holding the gauze out to its full width, and the like.

In the cotton trade, gauze and cloths of this character are standardized by taking a square and counting the number of threads per square inch. For example, a high-grade gauze carrying forty longitudinal and forty-four cross threads per square inch, carried eighty-four inches of thread.

For the most part the so-called manufacturers of surgical gauze purchase their supplies of woven gauze, gray or bleached, from the various mills of New England. These mills supply some nineteen grades, beginning with a gauze carrying twenty threads by ten, or thirty threads per square inch.

It should be noted that very little if any surgical gauze in the market is fully thirty-six inches in width. This is accounted for by the fact that these goods are woven in the gray thirty-six inches wide, and it is not practicable to bleach the goods, render them absorbent, and retain their full width. The usual variation is about one inch per yard; in other words, the average width will be found to be about thirty-five inches.

The following table shows the threads per inch, the average yardage per pound of the best known grades of surgical gauze:

SURGICAL GAUZE.

Threads per inch.	Yards per pound.
44 x 40	9.38
32 x 36	14.81
28 x 24	16.00
24 x 20	18.83
20 x 14	23.20

The National Formulary (First Edition), adopted as a standard two brands, Lehigh E. and Stillwater. These grades (now practically out of market) contained about sixty-four threads per square inch, and their weight was a little less than 800 grains to the square yard.

The nearest approach to a standardization of plain surgical gauze is one which I understand has been adopted by the Bureau of Municipal Research, which bureau is making an attempt to secure uniformity in the supplies for the various departments of New York City.

In respect to gauze the requirements are that the gauze shall count in the finished state not less than the total number of threads per square inch specified, shall not exceed the yardage per pound specified; it shall be free from loading, and shall be acceptable by the bureau as first quality in every respect. Gauze delivered under these specifications is required to be made from clean, white,

long cotton fibre, fully bleached and absorbent, of soft finish, and upon extraction with acidulated water (two per cent. hydrochloric acid) of not more than one per cent residue, and the reaction shall show no reaction for starch, soap, dextrin, glue or other filling.

The object of the foregoing test—extraction with acidulated water—is to prevent the addition of starch, soap, dextrin, or glue for making weight, increasing the apparent size of thread, etc.

This requirement would seem to be about as far as any standard could be expected to reach; indeed, the great variation in the requirements of the surgeon and the manifold mechanical household uses of gauze create a legitimate demand for a greatly varying material.

Mr. Geo. M. Beringer, Jr., in a paper heretofore cited, raises the question as to whether the Pharmacopœial recognition of medicated gauzes and surgical dressings would be a mistake. He states that it has been hinted that the pharmacist has not the facilities and training necessary for the preparation of surgical dressings, and he urges that this arraignment is not complimentary to the intelligence of the American pharmacist. He calls attention to the fact that the pharmacists of Germany, Austria, Sweden, Belgium, and elsewhere prepare such preparations from formulas in their respective pharmacopœias.

To my mind there is no question but that the pharmacist has the intelligence and perhaps the training necessary for the careful preparation of surgical dressings. It is not a question of can he, but will he take the care to properly prepare these dressings.

I have discussed this question at some length in a previous paper, in which the question was raised as to the relative fitness of the surgeon, the pharmacist and the manufacturer as makers and purveyors of surgical material. In this paper I stated that we may well claim for the American physician the highest of honors, we should all reverence the skill and genius of the American surgeon, yet it must be admitted that their offices are not as a rule the most suitable spot for the preparation of dressings. Contact with the clothing and person of patients carrying contagion of every name and kind, together with a thousand and one avenues through which the streams of infection may pour into their rooms, is evidence of the unfitness of the surroundings of the physician for the preparation of surgically clean dressings.

Likewise in hospitals, many of which are attached to medical

colleges, where students and operators carry infection from hundreds of sources of contagion, and where the dangers of infection can scarcely be avoided.

When dressings are prepared by the pharmacist the work is of necessity performed in the druggist's back room—a place which comes far short of conditions known as surgical cleanliness. The pharmacist, though ordinarily clean in person and habits in the pursuit of his calling, is far from aseptic. Like the physician, he is constantly in contact with infection through the person of his patrons.

In a few terse sentences Mr. Beringer attempts to convert the druggist's work table into a room suitable for the preparation of aseptic dressings. I doubt his ability, or the ability of the average pharmacist, to take these products into his own back room and produce therefrom sterile dressings. In advance, I would acknowledge my own inability to do so, notwithstanding a generation of experience along these lines, and should the necessity arise for an important operation in my own case, I certainly would reject dressings prepared either in a hospital, a physician's office, or the pharmacist's back room in favor of these made by a reliable manufacturer.

The facilities of the manufacturer whose whole organization is adapted to the production of surgical dressings are certainly more perfect than those of the surgeon to whom such work is only incidental; the employment of a room from which pathogenic organisms are entirely excluded is superior to the conditions in the hospital or doctor's office. Rooms in which no work is undertaken except the handling of aseptic material will certainly be more nearly surgically clean than a place where infection has constant access. Persons whose only calling is that of preparing surgical material, who have been trained in the principles underlying the disinfection of dressings, are much more competent to handle the same than the doctor's assistant to whom such work is of necessity relegated. Further, an organization devoted exclusively to the manufacture of dressings, once having the table arranged to prepare a yard of dressing, can produce any number of yards more perfectly than if done as occasion may require.

To the manufacturer and the dispensing pharmacist is due the credit of having made possible the convenient application of the principles of modern surgery.

Conclusion.

A summary of the thoughts embraced in the foregoing paper is as follows:

The rapidly changing conditions of surgical methods would not seem to warrant the insertion in the United States Pharmacopœia or in the National Formulary formula for the preparation of antiseptic surgical dressings. Any standard adopted for medication for surgical dressings would be liable to become valueless long before the next revision. A standard for antiseptic dressings once embodied in the Pharmacopœia would become complicated in the administration of food and drug laws by the constantly changing requirements of surgical practice.

It might be possible to establish official methods of assay by which antiseptic dressings could be judged. The standard for absorbent cotton in the eighth revision of the United States Pharmacopœia should be revised, and a standard is suggested herein. It would be possible to establish a standard by which surgical gauze and dressings made therefrom could be judged.

The principal requirements for surgical dressings made of cotton or gauze at the present time are purity and sterility; such dressings are known as plain aseptic dressings.

In the author's opinion, neither the facilities of the practicing physician, the hospital, nor those of the ordinary pharmacist are adequate for the preparation of dressings to meet modern requirements. The preparation of this class of material, like that of serums, toxins, and the like, requires special training and special facilities for their manufacture. Until economic conditions shall greatly change it is the author's opinion that the preparation of this class of material had best be relegated to those possessing the required facilities.

SOME QUERIES ON ALKALOIDAL ASSAY.

By W. A. Pearson, Philadelphia.

Much good work has been recently presented on alkaloidal assay, and it is reasonable to expect that much more satisfactory and accurate methods will be inserted in the next Pharmacopœia of the United States.

There are a few differences of opinion in regard to technic, however, that should be agreed upon before uniformity is to be expected.

Amount of Moisture in Drug.—Crude drugs are not as a rule assayed in the exact condition in which they are received. Frequently they must be dried before they can be ground and this loss of water may amount to as much as 30 per cent. Is it advisable to compute the results obtained to correspond to the original condition of the drug or to the moisture free basis?

Fineness of Powder.—It is well known that when a powder is ground, all of the particles are not of equal size and that if all the drug is ground and only the particles of a certain size are taken the sample will not be a representative one.

Would it therefore be advisable instead of stating that the powder should be of a certain fineness to state that it should be at least of a certain fineness or between certain limits of fineness?

Temperature.—In certain alkaloidal determinations the temperature plays an important part, in the results obtained. For example, in the assay of opium, the crystallization flask is directed to be set aside in a *moderately cool place.* No limits are given in U. S. P. for "moderately cool" and this temperature has been variously interpreted by different analysts. It is certain that much larger crystals are obtained near 0° C. than at slightly higher temperatures; it therefore seems important to ask what influence does temperature have upon the results of an alkaloidal assay?

Fumes.—Free alkaloids very readily combine with acids, and the analytical laboratory usually contains fumes of hydrochloric or nitric acids. Before the delicate titration of an alkaloidal residue is made there seems to be danger of these fumes combining with the alkaloid and lowering the results. To what extent do the fumes ordinarily present in the laboratory influence the results of an alkaloidal assay?

Indicators.—It has been claimed by the analysts in one lab-

oratory that cochineal is the best indicator for all alkaloidal titrations; the men in another laboratory prefer the general use of iodeosin. Does the indiscriminate use of these indicators give concordant results and would the assay be considered as being made according to the U. S. P. if an indicator not specified in the particular assay were used in the titration?

Color of End Point.—In all the alkaloidal titrations, the U. S. P. specifies that the standard solution should be added until a certain color is obtained. Owing to differences in judging the end point and the absence of a definite color standard a considerable variation is to be expected.

Ought not the end point of an alkaloidal titration be determined by matching a certain color of a standard chart under definite conditions?

Blank Determinations.—To avoid the difficulty of judging the color of the end point and to provide a check on the solutions being used a blank determination is usually made by the most analysts. Even this method is faulty where the alkaloidal residue still retains some color. Would it be advisable to specify that a blank test be made with every alkaloidal titration?

Amount of Solvent.—Most practical analysts who are regularly making alkaloidal assays are agreed that insufficient solvents are specified for extraction of alkaloids in many of the U. S. P. processes. For example, in the assay of Nux Vomica after oxidation of the Brucine the quantity of chloroform specified will not leave the supernate liquid clear nor will twice the specified quantity but by repeated extractions with chloroform the supernatant liquid will become clear. Is an assay made in accordance with U. S. P. process, when excessive quantities are used? If additional quantities of solvents are allowable, should each extraction be made until no precipitate is obtained with Mayers' reagent?

Identification of Alkaloids.—In the determination of alkaloids from crude drugs the U. S. P. makes no provision for the identification of alkaloids extracted. Would it be advisable to insert identification tests for the alkaloids after they have been extracted and estimated?

Physiological Tests.—After the alkaloids have been extracted and estimated, would it be advisable to insert physiological tests and determine the minimum lethal dose and note the characteristic action?

Conclusion.—In presenting the above queries I realize that I am presenting problems that can only be settled by extensive experimental work. The main practical question is to decide how great these various factors probably are and whether the necessary co-operative work is to be undertaken.

ANALYTICAL DEPARTMENT, SMITH, KLINE AND FRENCH CO.

THE TEACHING OF AND EXAMINATIONS IN PHARMACOGNOSY.[1]

BY HENRY KRAEMER.[2]

While it is true in teaching that success depends in large part upon the earnestness and personality of the teacher as well as his knowledge of the subject, much also depends upon the methods that are followed. It was the Agassiz method that developed a school of clear-headed and distinguished American zoölogists. Agassiz's words, "study nature, not books," ring true and are well worthy to be framed and hung up prominently in all laboratories. Some teachers feel that they would like to impress upon the students the facts which they have acquired or the point of view which they have attained. Others use some particular textbook and it is upon the facts that are to be gleaned from this that the student's efficiency is finally determined. A happier method is the one in which after certain fundamental principles have been mastered the teacher draws out from the student what he observes with the specimen in hand. Of course to the ordinary student this may be irksome as it is often difficult for him to discern the progress that has been made. It is also harder for the teacher, as in nearly every class there will be found some who are keen observers and likely to ask questions which require the teacher to admit that he does not know it all. It has usually seemed necessary in order to maintain discipline for the teacher to stick near his desk and the student to follow the exercises laid down. Happily

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[1] This is a continuation of a previous paper presented to this Association (see Proceedings, vol. 56, 1908, p. 672).

[2] Presented at the Boston Meeting of the American Pharmaceutical Association, August 17, 1911.

for all concerned we are approaching a condition when it is possible for student and teacher to work together, each receiving an inspiration from the other and each contributing to the *summum bonum* of knowledge. I have in a previous paper indicated what I consider to be the principal object in the study of Pharmacognosy as it relates to the training of the pharmacist. I said then that in view of the problems that confront us and that are constantly arising, the aim first should be the attainment of a knowledge of the characters of drugs rather than a general knowledge of them. The object of a course in Pharmacognosy is I take it not that a student shall examine so many drugs, but that he will be able to use his eyes so that he can determine whether a drug corresponds to a description, as that of the Pharmacopœia, whether the specimen is all of one kind, the quality of it, and similar practical questions when he is in business. We all know that a student usually examines but a small sample of the drug. His specimen may differ from that of his comrades in certain particulars, as in the case of Rhamnus Purshiana and this is confusing. But let him examine, say 5 or 10 pounds of this drug, and the characteristics will be so impressed upon him that he will be able to recognize even the fragments of it.

While at college a student can not possibly study thoroughly all of the drugs of the Pharmacopœia and National Formulary. I am beginning to be more and more impressed with the foreign method of teaching, in which the study is limited to a number of important drugs, or to such drugs as those the study of which has a didactic value and in the case of which the work is required to be well done. Let the students spend 3 or 4 hours upon each of the 22 important official drugs * and he will not only know these well, but he will find it comparatively easy to acquire a knowledge of other drugs under circumstances that will not make him confuse so many of them. I have in preceding years, because of the lack of time at my disposal considered from 6 to 10 drugs in the course

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* The following are the drugs that I include in the list of the 22 most important drugs of the Pharmacopœia: Acacia, Aconitum, Belladonnæ Folia, Cantharis, Capsicum, Cinchona, Cinchona Rubra, Digitalis, Ergota, Gentiana, Ipecacuanha, Jalapa, Lycopodium, Nux Vomica, Opium, Podophyllum, Quassia, Rhamnus Purshiana, Rheum, Senna, Sinapis Nigra, Strophanthus, Zingiber. Of course there are a few other drugs that might be considered equally as important as some of these by some teachers.

of a 2-hour period. The result was one of confusion to the student as was manifest in subsequent examinations. I find that students are better able to recognize crude drugs after they have handled a single lot during several hours, including the making of sections and the examination of them with the microscope.

During the session that a particular drug is being studied by the students it is a good thing to break up the monotony of the work by talking about the plant yielding the drug and if possible by having some growing specimens in a prominent place and in addition a herbarium specimen of the plant for each student. At the same time one can give some facts regarding the distribution of the plant, the history of the drug and its important constituents. In this way a student is enabled to concentrate himself upon a single drug, and thus the facts impress themselves and he acquires a knowledge of the drugs in a more natural way.

Permanent mounts of drugs should be at his command for purposes of microscopic comparison. The sections should be made by the student and these should not only be cross-sections, but tangential-longitudinal and radial-longitudinal as well. He should keep a record of his observations and make a series of drawings illustrating what he has seen, using both the simple microscope and the compound microscope. Sufficient assistance should be provided so that a student's questions may be answered and his specimens or slides examined, as he should not leave the laboratory without all doubtful points being made clear.

The powdered drug should be examined after the studies on the crude drug have been completed. It is surprising to see how the student views the whole subject after he has spent an afternoon first examining the crude drug with the naked eye and the aid of the simple microscope, then making sections and carrying on his studies with the compound microscope, and finally working with the powdered drug. He finds that the study of powdered drugs is not so difficult and furthermore, as in the study of Belladonnæ Folia an adulteration of poke leaves, is more readily determined in a powdered drug than in the crude drug. He finds as a matter of fact that one of the simplest methods in the examination of a number of drugs that may seem to be of good quality is to take 5 or 10 grams of the material selected from various portions of the lot, powder it in a small mill and examine the powder under the compound microscope. I have seen students again and again

find Poke Leaves in a sample of Belladonna Leaves that otherwise would have been pronounced of good quality. While we require students to make a permanent collection of the specimens of crude drugs which are furnished them for study, I feel that the time is at hand when we should require them to make a permanent collection of microscopic slides, illustrating these 22 important official drugs. As the compound microscope can be had at such a reasonable figure at the present time I think that every thing should be done to encourage students to invest in this piece of apparatus, as it is indispensable not only in detecting adulteration, but also in determining and establishing confidence in reliable jobbing houses.

EXAMINATIONS.

After the student has taken up the practical studies of vegetable drugs and has concentrated his attention on the most important of those that are official the question is What tests shall be applied to determine his qualifications to be a safe pharmacist? Of course, the professor has the advantage of seeing the student day after day, and if he has been faithful in attendance and has conscientiously carried on the work, the teacher must know his general ability after the entire course of instruction. Usually, however, an examination is given for the purpose of testing a candidate's knowledge of the subject. But what is the test of knowledge? What is the nature of the questions that are to be asked to test the candidate's knowledge in this particular branch? We have all been familiar during our college days with men who failed in examinations and who really knew more about the subject than some of those who passed the examinations. The secret of the latter in passing an examination very often consists really in concealing from the examiner what they do not know. If this is done discreetly and the student can impress upon the examiner what he does know he will probably pass the examination. There are some examinations where this can be rather easily done and this is particularly true of examinations in Materia Medica as conducted in most Colleges of Pharmacy and by Boards of Pharmacy.

In these examinations the memory test is largely relied upon. So much hinges upon giving the "Natural Orders," "Habitats," etc. The student preparing for these examinations usually uses some book in which in a series of parallel columns are given one or two words covering the information that is expected of him

in the examination. Partly because the subject of the examination is so lifeless, the student has never been stimulated in his studies. Furthermore because the examination is so perfunctory the student's thoughts are seldom carried beyond these parallel columns, and he can truthfully say that the whole subject is dry and uninteresting. Besides on this account the general inference is that the subject is of little or minor importance.

Occasionally we find teachers who dilate upon the subject of the history of drugs and the countries in which the plants are indigenous, but say practically nothing more of the drug than is contained in the Pharmacopœia. We find students who have had a good preparatory education who believe that in this knowledge they have valuable information to fit them to become retail pharmacists and usually they are very easily confused when it comes to the identification of specimens. Sometime ago I heard a judge of one of our city courts make some remarks in the course of an after dinner address that impressed me very much. He said: "The fact that you know that a certain drug is gathered in the Himalayas is not going to make you either a safe or successful druggist, you must know the nature and property of the substances you are handling and how safely to fill prescriptions and a good many other things that you only learn by experience." Any practical pharmacist knows this and yet the burden of most examinations in Materia Medica are upon questions that few teachers and examiners would pass an excellent examination upon without considerable study beforehand.

While the aim of an examination before a Board of Pharmacy appears to be to test a candidate's knowledge, the college examination should be with an additional object, viz., to round out the knowledge gained during the course and give the student self-reliance and confidence in himself. It should not be with the object of getting him ready to pass the Board of Pharmacy examinations as now conducted.

Now that the Boards of Pharmacy are seriously considering improving the methods of examination it seems to me that we might well ponder upon the subject and try to look at it from the point of view of testing a candidate's fitness to practice pharmacy. In my judgment we must eliminate the idea that because a professor gives an interesting historical lecture upon certain drugs it is expected that the student will have all of this information at his

fingers' ends. There are some things taught which make for the culture of the pharmacist and happy is the student who can sit under a professor that is learned and well balanced. There is something deeper and more important to the pharmacist than this general knowledge of drugs and that is a knowledge of the characters of the drugs which he handles in his practice. The history of each drug is exceedingly interesting, but this does not become a real part of a pharmacist's knowledge, save after many years of experience and reading, which he can do without the aid of a teacher, and when his horizon has been broadened. In one sense the same may be said of descriptions of plants yielding drugs. As in the learning of a foreign language we lay the foundation by first taking up the grammar of the subject and later taking up as much reading and study of its literature as time and inclination permit, so in the study of Pharmacognosy we first take up the specific characters and properties of a drug and then follow this by as much reading and study of a general character as we are able to do. There is, however, nothing stimulating and so far as I can see it, nothing useful in asking a question like the following: "Nux Vomica: (*a*) give habitat; (*b*) origin; (*c*) part used in medicine; (*d*) active principles; (*e*) official requirement." Ever since the days when I was a quizz master my conviction has been growing that questions of this type, which are asked on every hand, do more harm to the cause of teaching in pharmacy and to the development of professional pharmacy than is generally realized. Every man's knowledge must fit in this groove. There is no individuality to be developed, no increase in knowledge expected and no vitalizing influence in either the subject as taught or the examination which follows.

The following is another type of question that is asked in certain States by the Boards of Pharmacy and illustrates very forcibly the type of questions that should not be asked. The questions for the most part being confined to unimportant drugs and specifying the reading of certain books makes it obligatory upon the candidate to determine before taking the examination the books on which the examination is based. The following is a typical example: "What dose is given in Remington's Pharmacy, fifth edition, of the following: Rhus Glabra, is it considered a poison? (*b*) What is a minimum dose of Quercus, Rubus, Geranium? What is the common name of Convallaria? Name 22 incompatibles with mercuric

chloride (Corrosive Sublimate). There are 33. Name as the tenth edition of Potter's Materia Medica gives them. Does Potter's Materia Medica say Mercury is a tonic? Answer *Yes* or *No*. Does he say it is a poison? A purgative? From where is Veratrum obtained? And in action, is it related to Aconite in any form? Answer *Yes* or *No*. What is the average dose of Eucalyptus as given in Potter's Materia Medica, tenth edition?"

In addition to the slovenly construction of the questions and the veritable hodge-podge manner of associating the subjects I think it is quite clear how questions of this kind really hinder sound pharmaceutical education. I think students are to be pitied who have to run the gauntlet of such examinations in the various States, and the wonder really is that young men of education and good training are willing to come into the ranks of Pharmacy. It is quite clear on the face of it that the examiners who ask such questions are quite incompetent to fulfil their duties.

Of all subjects that are living, interesting, full of the greatest of possibilities and of the greatest of benefit to the professions involved, there is no subject that offers such a fertile field for the teacher and that can hold the interest of the student like that of pharmacognosy. I am quite aware that while my enthusiasm may be shared by some teachers my point of view may not have occurred to them. However, I would say that the teaching of pharmacognosy in its direct application to retail practice will prevail and if the examinations bring out the practical knowledge of the candidate we will find that the student will also have attained culture and those things that constitute the professional man.

I have often thought that it would be a good thing if Pharmacognosists could meet together occasionally and discuss not only methods of teaching, but the subject of examination questions. In order that we might improve our work and be able to utilize the results obtained by our colleagues in other colleges I have requested a number of professors to send me a set of model questions. I regret that there is not space for me to give all of these at this time. One professor has written stating that as his course consists entirely of laboratory work it does not involve questions. This is certainly novel and I should like to know how it is done. Apparently the professor relies entirely upon the students' work during the course. I feel that really every teacher ought to know before the end of the term the standing of every student, but I still feel as already

stated, that an examination should be held more for crystallizing out the thoughts of the students and the knowledge gained than for any other purpose. In other words, an examination should be in the nature of instruction to the student and should give him an opportunity of showing to what extent he has mastered the subject.

Professor Daniel Base has written in a spirit with which I heartily coincide, and I quote the following from his letter:

"I think State Boards would do well to confine questions in Materia Medica to the chief inorganic, vegetable and animal drugs and not ask questions about things with which the average pharmacist may have to do but once or twice in a year. The questions might reasonably involve a knowledge of botanical source, part official, when collected and why, description in correct terms, of the whole drug, drugs that resemble each other outwardly and how to distinguish them, the principal and some of the less important constituents, forms in which the drug is used, usual action of the drug, antidotes to principal poisonous drugs or their preparations, doses. I would advocate framing questions both in Board examinations and those of the college in such a manner as to test the candidate's thinking ability rather than his cramming powers. Perhaps this cannot be done so thoroughly in Materia Medica as in Chemistry or Pharmacy, because of the nature of Materia Medica, which necessitates memorizing to a greater extent than the other two subjects do. Examinations in Pharmacognosy, in addition to requiring the recognition of drugs from outward physical characters, taste, odor, fracture, chemical tests, etc., would properly require also microscopic knowledge, but I fear that the teaching and requirements in some States have not advanced to such a stage as that the Boards could be persuaded that the examinations should include microscopic work. In those advanced States in which the Boards would not hesitate to ask questions involving microscopic knowledge, I think the questions should be moderate and practical and perhaps along such lines as the following:

1. Relation between magnification and focal length.
2. Mounting of objects.
3. Familiarity with a few staining reagents, permanent and temporary.
4. Process of making a permanent mount with two differential stains.

5. Ability to recognize and name the different kinds of cells in a section.

6. Naming the kinds of cells in a powdered drug, especially such as stone, bast, tracheids, trichomes."

One of the questions in the list submitted by Professor G. H. Jensen strikes me as being very practical. It is "In the examination of a powder, what elementary structures place it into the class of barks, woods, and leaves?" Professor Albert Schneider has submitted a similar question which reads: "Name the tissues and tissue elements that are found in barks, and roots, in leaves, in seeds, in woods."

I also received a number of other lists of questions, but they did not strike me as having anything novel in them and so I do not give them at this time, although I will probably refer to them in another paper.

Professor Sayre has written in addition to sending me a list of questions some things that I feel like adding in concluding this paper. He says: "Permit me to state that you could not get ten men to agree on any set of questions nor to agree on the policy of making up the questions, but I venture to give you my own ideas in the limited time I have to dictate them offhand.

"In the first place, questions should have a carefully selected variety, that is, there should be a variety chosen from different classes of crude drugs. In the second place in almost every question something should be drawn out of the student in his answers as to the microscopical and, now and then, the botanical characteristics. Third, there should be sometimes added to the questions a general question rather than a specific one, such as 'Write a paragraph or a treatise of at least 250 words on what you know of a certain subject.' In the fourth place, I believe that examinations should represent modern thought and teaching and should include laboratory demonstrations where the student should have an opportunity to show, first, that he knows how to use the microscope, and second, that he has done microscopical work, and third, that he shall be able to demonstrate that he is familiar with certain microscopical processes. Fifth, I think that examinations in Materia Medica should be confined to well established and commonly recognized drugs."

In summarizing I may say then that in discussing this subject

of the teaching and examinations in Pharmacognosy that I have not been aiming to establish an ideal so much as to direct attention to the need of our considering our work from the standpoint of the practicing Pharmacist. There are many things that every Pharmacist should know, and these relate especially to the specific characters and properties of the important drugs. There are other things which he may know of certain drugs, and indeed, should know, to stimulate him in his professional work. But these are subjects that can be better handled in an oral examination than in written examinations. In Pharmacognosy we have a subject dealing with natural products and we should treat it in a natural way, instead of according to hard and fast lines and involving the framing of questions in the form of riddles or conundrums which depend for their solution upon so much memorizing rather than clear thinking and direct study of the drugs themselves, as we do in the study of other physical objects.

THE BOSTON MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

By M. I. Wilbert.

The Boston meeting of the American Pharmaceutical Association will long be remembered as one of the most eventful meetings in the history of that Association. This distinction will be given it not because of the superior nature of the programme offered or the unexpected announcement of an unusual scientific achievement, but because at this meeting the Association chose to break with the past and to engage in enterprises more or less new and untried so far as the organization itself is concerned.

Many, if not all the three hundred or more members of the American Pharmaceutical Association present at Boston no doubt expected and were therefore prepared for the developments announced in the course of the week and many, if not all of the members present were thoroughly in accord with the programme as outlined and wish the officers for the coming year well in the development of their pioneer work.

While the happenings at Boston were neither unexpected nor revolutionary in nature, they nevertheless entail changes in policies

and an entire recasting of the relations hitherto held by the American Pharmaceutical Association to the several branches of the drug trade and any predictions as to the ultimate outcome must necessarily be based on idle speculation.

A more comprehensive idea of the nature of the changes proposed can perhaps best be given by a more or less chronological report of the proceedings as reflected at the several sessions of the Association attended by one individual.

The first general session of the 59th annual meeting of the American Pharmaceutical Association was called to order by President Eberle shortly after 3 o'clock on August 14, 1911, at the Hotel Vendome. After a few preliminary remarks by the president and a short prayer by Rev. A. R. Williams, of East Boston, the Lieutenant-Governor of the State of Massachusetts, Louis A. Frothingham, welcomed the Association on behalf of the State, and the acting Mayor of Boston, Walter L. Collins, offered the hospitalities of the City of Boston.

These addresses of welcome were replied to by R. H. Walker of Gonzalez, Texas, who called attention to some of the advantages of membership in the A. Ph. A.

George S. Smith, in a short and interesting address, called attention to a number of facts regarding the commercial importance of Boston and the surrounding towns and pointed out that few sections of the country are as thickly populated as is the territory adjacent to and more or less dependent on the City of Boston.

C. H. Packard, on behalf of the druggists of the Boston district, extended to the members of the American Pharmaceutical Association, their relatives and friends, a hearty welcome to the Hub.

These several addresses were replied to by C. M. Ford of Denver, who in a facetious address reminded the members that the time had come for them to again think of visiting the central portion of the United States and he, therefore, extended an invitation to meet in the City of Denver in 1912.

The annual address of the president called attention to many of the shortcomings and needs of those engaged in the drug and apothecary business and contained a number of suggestions for bringing about changes in present-day conditions. The greater portion of the address was subsequently referred to a committee of five members, while the recommendations referring to legislation

were referred to the Section on Education and Legislation for further discussion.

The felicitations of the members of the N. W. D. A. were presented by Fred. L. Carter, and the greetings of the N. A. R. D. were presented by F. C. Godbold. Dr. R. H. Hatcher extended the good wishes of members of the American Medical Association, M. I. Wilbert presented the felicitations of the Surgeon-General of the Public Health and Marine-Hospital Service and Prof. José P. Alacán presented greetings from the pharmacists of Cuba.

The second general session of the Association was largely devoted to reports of committees and the annual reports of the officers of the Association. A rather unusual diversion from the routine nature of these reports was the announcement made by Jos. P. Remington, as Chairman of the Committee of Revision of the Pharmacopœia of the United States, that the report of the Sub-Committee on Scope had finally been acted on by the members of the executive committee and that he was now prepared to give publicity to the final decisions on the scope of the U. S. P. IX. He then introduced Dr. Solomon Solis-Cohen, who as the invited guest of the Association, presented an interesting and well rounded address in which he discussed the influence of the U. S. P. on the practice of medicine. This address was enthusiastically received and the general conclusion that the Pharmacopœia of the United States should contain formulas or descriptions for "all preparations that can be used to advantage in caring for the sick" is so obviously sane that it will no doubt receive the endorsement of all well meaning pharmacists as well as all seriously minded physicians.

This address was commented on by a number of members present and, on motion, it was agreed to give wide-spread publicity to the same. It was resolved to have the address printed in pamphlet form and distributed among medical practitioners.

The committee on nominations gave out the following names for officers to be elected by a mail ballot during the year: For president, W. B. Day of Chicago; Charles Holzhauer of Newark, N. J.; William Mittelbach of Boonsville, Mo.; for vice-president, José P. Alacán of Havana, Cuba; C. M. Ford of Denver, Col.; Otto F. Claus of St. Louis; R. H. Walker of Gonzales, Texas; C. A. Mayo of New York; W. J. Teeters of Iowa City, Iowa; J. O. Burke of Nashville, Tenn.; and A. H. Clark of Chicago; for council, F. C. Godbold of New Orleans; W. C. Alpers of New

York; George B. Kauffman of Columbus, Ohio; C. W. Johnson of Seattle, Wash.; L. E. Sayre of Lawrence, Kansas; E. Berger of Tampa, Fla.; J. C. Wallace of New Castle, Pa.; F. W. Meissner, Jr., of La Porte, Ind.

The sessions of the several sections were, in many instances at least, held simultaneously and the precedent established in previous years is now thoroughly well established and will in time, no doubt, lead to the shortening of the time required for the annual meeting of the Association, so as to make these annual gatherings of greater interest and value to the really busy men in our calling.

SECTION ON SCIENTIFIC PAPERS.

At the first session of the Section on Scientific Papers which was held on Tuesday afternoon simultaneously with the first session of the Section on Commercial Interests, a radical modification in the By-laws of the section was proposed by Chairman Clark and endorsed by the members present. These changes were subsequently endorsed by the Council of the Association and the necessary changes in the By-laws of the Association were acceded to at the concluding general session. In future the Section on Scientific Papers will be in position to conduct its business independently of the other sections and will therefore have sufficient time to discuss all of the communications read at the several sessions.

This year there were upwards of 25 papers to be presented at two sessions of the section, and the time, as usual, was wholly inadequate to present and discuss more than half of this number. Not any of the papers were printed in advance of the meeting and this no doubt was an additional reason why so few of the papers were discussed at length. As an additional proof of this statement it is but necessary to point out that the Report of the Committee on Drug Market, August, 1911, which was available in printed form, not only elicited considerable discussion, but also gave an opportunity for correcting several statements objected to by some of the members present.

Among the papers presented at this section that were at all discussed are the following:

The Pharmacopœial Standard for Desiccated Thyroid Glands, by Hunt and Seidell.—The authors proposed a standard iodine content, 0.2 per cent., with a maximum variation of 0.03 per cent. above or below this figure. The limit for moisture is placed at

6 per cent., and that for ash at 5 per cent. Several of the members present expressed the belief that this standard was high, and that an iodine content of 0.15 per cent. would be more in keeping with the available product.

The Preparation, Quality and Testing of Quinine Tannate.—Puckner and Warren, under this heading, discussed the requirements made for quinine tannate in many of the foreign Pharmacopœias and reported a systematic examination of the product available in this country, giving the names of manufacturers, the degree of purity of their quinine tannate and the various contaminations. This paper was discussed to some extent, and on motion a majority of the members present voted to delete the names of the manufacturers from the paper as printed in the journal of the Association.

Alkaloidal Assaying.—The assay processes of the U. S. P. were more or less systematically discussed by Messrs. Stevens, Dohme, Gordin and others. The subject-matter under discussion was subsequently referred to the U. S. P. Committee of Revision, and was further discussed by the Sub-Committee on Assay Processes.

Gelsemium Alkaloids.—L. E. Sayre presented an additional communication on the alkaloids of gelsemium, and proposed the renaming of the several alkaloids. This communication led to a general discussion on the misleading names applied by manufacturers to some of the rarer alkaloids, but the members of the section were apparently not willing to commit themselves to any definite policy for correcting existing abuses.

Physiological Standardization.—The physiological standardization of drugs was discussed by Messrs. Haskell, Vanderkleed, Edmunds and others. Chas. C. Haskell reported a number of experiments on physiological drug-testing, and in connection with digitalis recommended the use of the one-hour frog method, as outlined by Edmunds and Hale in Bulletin No. 48 of the Hygienic Laboratory, Public Health and Marine-Hospital Service of the United States. Chas. H. Vanderkleed presented a paper in which he recommended the guinea-pig method, described by Reed and Vanderkleed in a previous paper on the subject.

Capsicum.—Wilbur L. Scoville presented a Note on Capsicum, showing the great variation in the strength of capsicum, and suggesting the possibility of the pungency of this drug being used as a simple test for quality. This paper elicited some discussion in

the course of which it was pointed out that the physiological test for capsicum was infinitely more delicate and more reliable than the similar test that has been proposed for use in connection with aconite.

Aconite.—William Mansfield exhibited a number of samples of commercial aconite, discussed the varying qualities now coming into this market, and proposed that the stem crowned root alone be described in the Pharmacopœia of the United States, maintaining that the bud crowned root could be utilized for propagating or continuing the plant.

Ash Content of Drugs.—M. I. Wilbert presented a compilation of data on pharmacopœial limitations of the ash content of drugs, and pointed out that this factor could not at the present time be utilized to advantage. The discussion emphasized the need for permitting rather wide variation in the ash limitation of drugs, particularly in connection with root and leaf drugs.

Permanency of Some Astringent Preparations was discussed by W. L. Scoville, who reported the systematic examination of twenty fluidextracts of drugs containing tannin, during a period of three years. He outlined his method of examining the preparations and laid emphasis on the desirability of using strongly alcoholic menstrua for drugs of this class.

The officers of this section for the coming year are W. O. Richtmann, Satsuma Heights, Fla., Chairman; and C. H. LaWall, Philadelphia, Pa., Secretary.

SECTION ON COMMERCIAL INTERESTS.

The Section on Commercial Interests held two sessions. Franklin M. Apple, the Chairman of the Section, was obliged to leave before the opening session because of sudden bereavement in the family, and B. E. Pritchard, of Pittsburgh, presided. Many of the papers presented at this section were discussed quite exhaustively and the immediate results will no doubt be beneficial.

Among the papers that were read and discussed were the following:

Commercial Monopoly—A Hindrance to Progress in Materia Medica Science, was the title of a paper by F. E. Stewart, in which he discussed at some length the relation of product and process patents to scientific development of medicine.

The Principles and Practices of Bookkeeping were discussed

by Hy. P. Hynson, who commented on some of the shortcomings of the commercial courses taught in colleges of pharmacy. Several additional papers along the same lines were presented, one by Ambrose Hunsberger on Simplified Accurate Methods of Recording Charge Sales, and one by E. Fullerton Cook on the Cost of Conducting Drug Business.

Window Displays were discussed by B. E. Pritchard, who commented on the practices of one of the large drug concerns in Pittsburgh; and in a paper along similar lines by Otto Raubenheimer, who discussed Pharmaceutical Window Displays and commented adversely on some of the objectionable displays that he has observed from time to time.

C. M. Ford presented some comments on the trend of modern pharmacy, and incidentally described a system of drug-store inspection that is being introduced in the City of Denver.

SECTION ON PRACTICAL PHARMACY AND DISPENSING.

The Section on Practical Pharmacy and Dispensing, with Louis Saalbach of Pittsburgh, Pa., as Chairman, also held two sessions, at which a number of practical pharmaceutical problems were discussed.

The Color of Tincture of Iron Citro-Chloride was discussed by Otto Raubenheimer, who exhibited a number of samples comparing the National Formulary product with samples made according to other formulas.

A Few Questions Suggested by Comparison of the National Pharmacopœias was the title of a paper by Oscar Oldberg. This paper, in the absence of the author, was read by the Secretary of the Section. Oldberg discussed the desirability of establishing a Section on the Pharmacopœia so that matters relating to the Pharmacopœia could be discussed without interfering with other more or less diverting papers.

Infusion of Digitalis was discussed by Chas. M. Ford and J. Leon Lascoff. Both of these authors pointed out the need for making this preparation extemporaneously from a good quality of leaf. The discussion following the reading of these papers was spirited and at times acrimonious, evidencing considerable variation of opinion as to the objects sought to be attained by the addition of alcohol to the infusion. There was also some difference of opinion regarding the preferable method of keeping digitalis.

A New Color for Pharmaceutical Preparations was described by Chas. H. LaWall, of Philadelphia, Pa., who called attention to some of the possibilities of sulphonated orcein or vegetable red, a coloring matter now widely used by confectioners. This paper elicited considerable discussion on the standardization of colors, in the course of which Otto Raubenheimer exhibited a French publication or code of colors that has been adopted as a standard for color for a variety of purposes.

Sanitation in Pharmacy was discussed by J. Leon Lascoff, who proposed the sterilization of bottles returned to the pharmacy. This led to a rather spirited discussion on the possible abuses that might arise in this connection, many of the members believing that medicine bottles should not be used over again under any pretense.

A Plea for More Working Formulas for Chemicals in the U. S. P., by W. H. Glover, was discussed at some length and the question was finally referred to the Committee on Recipe-Book.

The officers of this section for the ensuing year are P. Henry Utech, Meadville, Pa., Chairman; Wm. A. Hall, Detroit, Mich., Secretary.

SECTION ON EDUCATION AND LEGISLATION.

The Section on Education and Legislation, as usual, held three sessions. The first was presided over by Chairman Charles W. Johnson, who in his address as chairman discussed the desirability of solving the problems of pharmaceutical education. The report of the Secretary, Wilbur J. Teeters, was a comprehensive review of legislation proposed and enacted in the several states. On motion of H. L. Taylor the Secretary was complimented for his comprehensive compilation, and it was further suggested that the section continue the collection of material of this kind.

H. L. Taylor presented a report of the Syllabus Committee which was commented on by E. Fullerton Cook, in a paper on Commercial Training as Outlined in the Syllabus. The shortcomings of the Syllabus were further commented on by C. B. Lowe and others, several of the members taking advantage of the occasion to point out that the Syllabus was in course of evolution, and that the next edition would no doubt be much more perfect than the one now available.

Hy. P. Hynson presented a paper on the Real Educational Needs of the Pharmacist, in the course of which he called atten-

tion to many of the shortcomings in the present-day curriculum of pharmaceutical schools.

The second session of the section was presided over by John C. Wallace of New Castle, Pa., and was generally commented on as being one of the most interesting sessions of the Boston meeting.

The third session, following the established precedent, was a joint session of the section with the National Association of Boards of Pharmacy and American Conference of Pharmaceutical Faculties, at which a number of questions relating to state board examinations were discussed at length.

The officers of this section for the ensuing year are John C. Wallace, New Castle, Pa., Chairman; Wilbur J. Teeters, Iowa City, Iowa, Secretary.

SECTION ON HISTORICAL PHARMACY.

The Section on Historical Pharmacy held two sessions this year, or perhaps more correctly, one session in the afternoon, on the boat returning from Plymouth, and an adjourned session, at the hotel, in the evening. The Chairman of the Section, Joseph L. Lemberger, presided and the programme was replete with interesting subjects. Among the several contributions offered at the afternoon session was the presentation of a scrap-book entitled Hallbergana, by Francis B. Hays of New York. This book contains an interesting collection of material, historical, biographical and otherwise, relating to the late editor of the *Bulletin of the American Pharmaceutical Association,* C. S. N. Hallberg.

At the evening session several additional contributions were presented, among them an illustrated lecture on The Apothecary in Literature, by Edward Kremers. This contribution was a real treat, and thoroughly well appreciated by all who had the privilege of listening to the lecture, and seeing the pictures exhibited by the lecturer.

ADDITIONAL SESSIONS OF THE ASSOCIATION.

In addition to the two general sessions announced on the programme, the Association held a special session on the morning of Wednesday, August 16, at which several Committee reports were received. Another special session was held on Friday afternoon, preceding the meeting of the Section on Historical Pharmacy. The object of this session was to determine the place of meeting for

1912. After considerable discussion Denver was by vote of the members present selected as the place of meeting. The association at this session also adopted a resolution, offered by Joseph P. Remington, endorsing the spirit and the letter of the Pure Food and Drugs Law, and commending Dr. H. W. Wiley for the methods followed by him in enforcing this law. A third special session of the Association was held Friday evening after the adjourned meeting of the Section on Historical Pharmacy. This session was called for the purpose of presenting a number of changes in the By-laws of the Association, providing for the change in the nature of the publications of the Association, the changes necessitated by the By-laws adopted by the Section on Scientific Papers, and also a change in the By-laws providing for the transference of the beginning of the fiscal year of the Association from July to January, and an increase in the salaries of a number of the paid officials of the Association. At the final session of the Association on Saturday morning these several changes were endorsed, and at the conclusion of this session John G. Godding of Boston, President, and the remaining officers for the ensuing year were installed.

The Council of the Association announced the election of H. M. Whelpley of St. Louis, as Treasurer; James H. Beal of Scio, Ohio, General Secretary and Editor; Henry Biroth of Chicago, Honorary President; E. G. Eberle of Dallas, Texas, Chairman of the Council, and Joseph W. England of Philadelphia, Pa., Secretary.

The outgoing officers of the Association were given a vote of thanks for the efficient manner in which they had conducted the business of the Association, and the Boston pharmacists and others who had contributed to the success of the meeting were also given a vote of thanks. It was generally agreed among the members present that whatever uncertainty there might be regarding the future of the Association, there could be no mistaking the fact that the Boston pharmacists and Bostonians generally had proven themselves to be royal entertainers, and that so far as the social events of the annual gatherings might be concerned the Fifty-ninth Annual Meeting of the American Pharmaceutical Association will long be remembered as one of the most pleasant, and socially the most successful that the American Pharmaceutical Association has ever held.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACOLOGY AND MATERIA MEDICA.

By M. I. Wilbert, Washington, D. C.

The past three months have been replete with happenings of interest to the various branches of the drug trade, and it would be difficult indeed to even attempt to accurately reflect, in a limited number of pages, the many and varied influences that are at work at the present time to bring about an improvement of conditions in the drug business.

The literature of the quarter is extensive, and it will be impracticable to call attention to more than a few of the more important publications.

Volume 58 of the Proceedings of the American Pharmaceutical Association has finally been distributed, and while, for a number of reasons, no doubt, the publication of the book has been unusually delayed, the resulting volume is the largest, and in some respects the most valuable, that has appeared up to the present time.

The book contains a total of nearly 1500 pages, and in the report on the Progress of Pharmacy and the many original contributions presented therein adequately reflects the present-day status of Pharmacy.

The Proceedings of the Tenth International Congress of Pharmacy, held at Brussels, September 1 to 6, 1910, have been published, and constitute a large 8vo volume of xlix and 454 pages, with numerous illustrations. The list of members includes the names of upward of six hundred persons more or less well known in pharmaceutical circles abroad. The number of American subscribers is disappointingly small, and serves to emphasize the frequently made assertion that in matters relating to the progress of the sciences of pharmacy this country does not take the comparatively advanced position occupied in medicine and many other lines.

Pharmacopœial Publicity.—An editorial note, commenting on the evident non-compliance with the U. S. P. Convention instruction to give publicity to the progress of the work of revision, expresses doubt as to whether the instruction has been forgotten or neglected or whether it was in the nature of a political promise, and

concludes that a statement on this subject from the committee to the pharmaceutical press of the country would undoubtedly be welcome.—*N. A. R. D. Notes,* 1911, v. 12, p. 904.

German Pharmacopœia.—The now official fifth issue or fifth edition of the German Pharmacopœia is still being discussed and actively criticized in all the well-known pharmaceutical journals. The objects and the uses of this pharmacopœia are not generally recognized, particularly in America, and reviewers in this country frequently criticize the scope and contents of the German Pharmacopœia from a strictly American point of view, forgetting that our own U. S. P., while theoretically a complete and highly commendable work, is a sealed book to many, if not the majority, of retail druggists, and that comparatively few are in a position to or capable of applying the various tests embodied in the U. S. P.

The German Pharmacopœia, on the other hand, is the standard guide for the apothecary, who is by law compelled to comply with all of its requirements. A book review (*J. Am. M. Assoc.,* 1911, v. 56, p. 1218), commenting on this feature of the German Pharmacopœia, points out that this book "is an indication of the services that can and should be rendered by pharmacists for controlling the identity and purity of drugs used in the treatment of diseases."

Japanese Pharmacopœia.—A news note (*Chem. and Drug.,* July 29, 1911, p. 140) points out that the Japanese Pharmacopœia is to be issued in a revised form at the end of 1915. The present edition is being unfavorably criticized.

American Chemical Society.—The summer meeting of the American Chemical Society was held in Indianapolis, June 28 to 30, and is reported to have been an unusually successful meeting. In point of view of attendance it is said to have been the largest summer meeting that the Society has ever held. The Division of Pharmaceutical Chemistry held three sessions, at which a number of pharmacopœial subjects were discussed, the suggestions, in several instances, being referred to the Pharmacopœial Revision Committee for further consideration.—*J. Ind. and Eng. Chem.,* 1911, v. 3, pp. 610–614.

International Association of Chemical Societies.—On April 25, 1911, a preliminary meeting of delegates from a number of European chemical societies met in Paris for the purpose of organizing an international association of chemical societies for the purpose of considering chemical problems of general or inter-

national interest. The work of the association is to consist largely in the nomination of commissions in charge of studying questions submitted to them.

The American Chemical Society, at the recent meeting in Indianapolis, signified its willingness to affiliate, and empowered the president of the society to enter into correspondence with the proper officials to learn the details regarding the proposed organization.—*J. Ind. and Eng. Chem.*, 1911, v. 3, p. 614.

International Pharmaceutical Federation.—An editorial (*Pharm. J.*, London, 1911, v. 87, p. 32) comments on the organization of the International Pharmaceutical Federation, recently completed at The Hague, and points out that in addition to strictly scientific subjects it is proposed to exert a beneficial influence on such subjects as the international arrangements relating to patents and trademarks and commercial treaties affecting matters of this kind. This organization appears to have attracted considerable attention on the continent of Europe, despite the fact that in English-speaking countries the objects and the possibilities of coöperation on the part of pharmaceutical organizations have received little or no consideration.

American Medical Association.—The Los Angeles meeting of the American Medical Association, while not as largely attended as some immediately preceding it, will no doubt prove to have been an important one from many points of view. Not the least important of the several accomplishments of this meeting was the election of the nestor of American medicine, Dr. Abraham Jacobi, to serve as president of the Association. An editorial (*J. Am. M. Assoc.*, 1911, v. 57, p. 122), commenting on his election, asserts that "few if any men in the American medical world to-day can look back on as active a life as that of Jacobi. As a teacher, practitioner, and worker in medical organizations he has been a leader for half a century."

An editorial (*Pacific Pharmacist*, July, 1910, v. 5, p. 83), in commenting on the meeting of the American Medical Association, asserts that the matter of dispensing physicians, counter-prescribing druggists, prescription percentage evil, selling and prescribing patent and fake remedies, and the U. S. P. and N. F. propaganda were warmly discussed. Physicians very frankly admitted that they knew little or nothing about drugs and urged better courses of instruction in materia medica for the medical colleges.

The report of the reference committee on sections endorsed a resolution, regarding trade-marks and patents, referred by the Section on Pharmacology and Therapeutics, and also presented a number of recommendations submitted in the address of the chairman of the delegation from the American Pharmaceutical Association. Not the least important of the several recommendations is the one relating to the education of pharmacists, embodying the suggestion that "Such education should include ethical instruction as well as instruction in the branches usually included in the courses given by colleges of pharmacy."

The report of the reference committee on medical education, in commenting on the work done by the Council on Pharmacy and Chemistry with reference to simplifying the requirements of instruction about drugs in the Pharmacopœia, says: "Everybody admits that valuable time is wasted in giving instruction about useless drugs because they appear in the Pharmacopœia and because state licensing boards are liable to ask about them."—*J. Am. M. Assoc.*, 1911, v. 57, p. 132.

Medical Education.—A recent number of the *Journal of the American Medical Association* (Aug. 19, 1911, v. 57, pp. 630 ff.) presents a description of the medical colleges in the United States and Canada. Accompanying editorials (pp. 654 and 658) discuss the progress that has been made, under the auspices of the Council on Medical Education of the American Medical Association, during the past seven years. During this period the number of medical colleges has been reduced from 166 in 1904 to 120 at the present time. The number of graduates during the same period of time has been reduced from 5747 in 1904 to 4273 in 1911. The amount of money given for medical education has increased from a few thousands of dollars during 1904 to several millions of dollars during the last year.

British Pharmaceutical Conference.—The forty-eighth annual meeting of the British Conference was held at Portsmouth, the opening session being called to order by the president, Mr. W. F. Wells, of Dublin, on the morning of July 25, 1911.

The presidential address dealt mainly with the pharmacy laws of Great Britain and Ireland, with some references as to how they differed from similar laws in Germany and France. The proceedings of the Conference were this year divided into two sections,

Science and Practice, the new arrangement evidently meeting with the approval of the members present.

The papers read in the Science Section are quite up to the usual high standard of the communications presented to this organization, and many of them are on subjects of immediate practical interest. The papers are, as usual, reproduced entire in the current numbers of the British pharmaceutical journals. At the closing session on Thursday, Sir Edward Evans was elected president for the ensuing year.

American Pharmaceutical Association.—The fifty-ninth annual meeting of the American Pharmaceutical Association, held in the City of Boston, August 14 to 19, 1911, will no doubt prove to have been epoch-making for American pharmacy, as the changes in policies that are involved must necessarily bring about a more or less complete modification of the relations existing between the Association and the several branches of the drug trade represented in its membership.

Just what the future has in store for the Association would be difficult indeed to prophesy, but, with its long and honorable history as an incentive, the present and future officers must and will continue along the lines of progress so thoroughly well defined by the founders and the Association.

Whatever differences of opinion may be evidenced regarding the immediate success of the new enterprises, there can be no difference of opinion regarding the abilities of Boston pharmacists as entertainers. Members of the Association from far and near were pleased with the completeness of the preparations for the meeting, and it was generally agreed that few cities can equal and none can excel the City of Boston as a meeting place for the American Pharmaceutical Association.

Dr. H. W. Wiley and the Food and Drugs Act.—Few happenings during recent months have attracted more widespread attention than the controversy that has grown out of a technical infraction of the law by Dr. H. W. Wiley and some of his associates in securing the services of Dr. H. H. Rusby as an expert in connection with the examination of drugs imported at the port of New York. The House Committee on expenditures in the Agricultural Department has conducted an exhaustive investigation regarding the origin and nature of the controversy, and the members

of this committee will no doubt be in position to submit a satisfactory report to Congress at its next meeting.

To Dr. Wiley and his friends the unanimity with which the various periodicals and organizations have espoused his side of the controversy is indeed gratifying, and presages the appreciation that many thinking persons have of his work.

Pure Drugs and Medicines.—Virgil Coblentz discusses the general results of the analysis of two hundred and thirty prescriptions made by him for the New York *World,* and concludes that, if druggists would buy only from reliable firms and employ competent, conscientious assistants, they would be in position to render such service as the public has a right to expect.—*J. Ind. and Eng. Chem.,* 1911, v. 3, pp. 540–542.

Pharmaceutical Specialties.—An editorial points out that American pharmaceutical houses are apparently content to devote their energies to the devising of "pharmaceutical specialties," mere mixtures of well-known medicaments, that are designed to be attractive to both the eye and the palate, and are usually provided with names that are meaningless or, more often, therapeutically suggestive. The editorial concludes with the assertion that the credit accruing to our pharmaceutical manufacturers is discouragingly small; in fact, it is no exaggeration to say that the average American "pharmaceutical specialty" is not only of no benefit to medicine or pharmacy, but is a distinct handicap and detriment to both professions.—*J. Am. M. Assoc.,* 1911, v. 57, p. 576.

Nomenclature.—A recent editorial in the *American Druggist and Pharmaceutical Record* (July 10, 1911), on similarity in pharmaceutical nomenclature, has been reprinted in the *Pharmaceutical Journal* (London, July 29, 1911, p. 133) and is being freely commented on by pharmacists. The proposition to have an international committee which would take into consideration the whole question of pharmacopœial and pharmaceutical nomenclature is an eminently laudable one, and should receive the endorsement of every active pharmacist.

Acidol.—This is described by the Council on Pharmacy and Chemistry as betaine hydrochloride, $C_5H_{11}NO_2HCl$, occurring as colorless crystals freely soluble in water. It contains 23.8 per cent. of absolute hydrochloric acid.—*J. Am. M. Assoc.,* 1911, v. 57, p. 396.

Angelica Oil.—Bolcker and Hahn, by a series of fractional distillations of essential oil of angelica, have succeeded in isolating a

new constituent (*Apotheker Zeitung*, 1911, 219). It is a lactone of the formula $C_{15}H_{16}O_3$, melting at 83° and boiling at 250° at 250 mm. pressure. It forms a di-brom addition product, $C_{15}H_{16}O_3Br_2$. On heating with alcoholic potash, it gives the potassium salt of the oxyacid $C_{15}H_{18}O_4$.—*Chem. and Drug.*, July 29, 1911, p. 164.

Digitalis.—S. Hirohashi presents the results of a study of the quantitative valuation of digitalis, in which he reports his results with the Focke method, using a Japanese variety of *Rana esculenta.* These results would indicate that an infusion strained through muslin is more active than the corresponding preparation filtered through paper.—*J. Pharm. Soc., Japan,* July, 1911.

The Chemistry of Ethyl Ether.—Baskerville and Hamor present the results of a comprehensive study on the chemistry of ethyl ether, including a comprehensive bibliography. The report includes observations on the changes which occur in ethyl ether during storage, the action of oxygen on ether, the detection of peroxides in ethyl ether, and a scheme for the examination of ethyl ether for analytical and anæsthetic purposes, with particular reference to the detection of avoidable impurities.—*J. Ind. and Eng. Chem.*, 1911, v. 3, pp. 378–398.

Baskerville, in a review of the chemistry of anæsthetics, points out that American official ethers call for three to four per cent. of ethyl alcohol, in accordance with an old and erroneous theory that alcohol protects the ether. Alcohol is practically never free from water, and in the presence of water and oxygen forms oxidation products.

Hegonin.—This is described as silver nitrate ammonia albumose, obtained by treating silver ammonium nitrate with albumose. Hegonin is said to contain approximately 7 per cent. of organically combined silver. It occurs as a light-brown powder readily soluble in water. Its aqueous solutions do not coagulate albumin, even on heating, nor are they precipitated by sodium chloride.—*J. Am. M. Assoc.*, 1911, v. 57, p. 396.

Hexamekol.—A news note (*Chem. and Drug.*, July 29, 1911, p. 164) points out that hexamekol is a combination of guaiacol and hexamethylenetetramine. It forms a white crystalline powder, and contains 65 per cent. of guaiacol.

Hormonal.—Peristaltic Hormone-Zuelzer is a liquid extract obtained from the spleen of an animal killed at the height of digestion. Hormonal is a yellowish liquid which is often turbid,

but it is claimed that the slight flocculent precipitate does not affect its efficiency. It is claimed that hormonal has the property of exciting the peristalsis of the intestine and provoking the evacuation of the fæces. Its use is still in the experimental stage.—*J. Am. M. Assoc.*, 1911, v. 57, p. 291.

Maretin.—W. Heubner protests against some of the advertising literature recently sent out by the firm making maretin. He asserts that this substance has a powerful action on the blood, and is far from being the harmless medicament that it is claimed to be by the manufacturer.—*Therap. Monatsh.*, 1911, v. 25, pp. 364–368.

A correction by Dresser is published in the same journal (August, pp. 472–475), and in a reply by Heubner (pp. 476–479) the latter reiterates his belief that maretin is not a safe remedy.

Liquid nitrous oxide, or dinitrogen monoxide, N_2O, in the liquid state, is described by the Council on Pharmacy and Chemistry as a colorless mobile liquid, boiling at 89.8° C., solidifying at —102° C., and having a specific gravity of 0.937 at 0° C. Liquid nitrous oxide returns to the gaseous state when the pressure is reduced and the temperature raised. A number of chemical tests to which the substance should respond are given and its actions and uses are discussed.—*J. Am. M. Assoc.*, 1911, v. 57, p. 563.

Tincture of Opium.—Farr and Wright, in a paper on The Supposed Loss of Morphine in the Preparation of Tincture of Opium, proved by experiments that the loss is real, and varies from 0.8 to 9 per cent. of morphine, with an average of 4.78. The authors suggest that the loss is due to occlusion of the alkaloid in the opium, but they are making further experiments.—*Chem. and Drug.*, July 29, 1911, p. 151.

Oxygen.—Baskerville and Stevenson present a critical study of the bibliography, methods of preparation, and methods of analysis of oxygen, and outline standards of purity recommended for oxygen to be used in medicine. They conclude that the gas should be neutral toward moist, delicate litmus paper; and when passed through an aqueous solution of silver nitrate it should produce no turbidity.—*J. Ind. and Eng. Chem.*, 1911, v. 3, pp. 471–476.

Saccharin.—An unsigned note, commenting on the proposed restricting of the use of saccharin in food, as outline in food inspection decision 135, asserts that 0.3 gramme of saccharin possesses the sweetening power of 165 grammes of cane sugar, and points out that it is hardly conceivable that any one person would daily digest

such an amount of saccharin in food and beverage.—*J. Ind. and Eng. Chem.*, 1911, v. 3, p. 438.

Scarlet R, Medicinal Biebrich, is amido-azo-toluol-betanaphthol, and occurs as a dark brownish-red powder nearly insoluble in water, slightly soluble in benzene and acetone, and easily soluble in chloroform, oils, fats, and phenols. It is slightly soluble in cold alcohol and somewhat more soluble in hot alcohol. It is generally used in the form of ointment, and is said to be useful in stimulating the proliferation of epithelial cells.—*J. Am. M. Assoc.*, 1911, v. 57, p. 291.

Thyroid Standard.—Bennett, R. R., in a paper on the standardization of dried thyroid gland, suggests that it should be done on the basis of 0.15 per cent. of iodine, and describes Baumann's method for determining the iodine. It appears that the iodine standard is most commonly used commercially.—*Chem. and Drug.*, July 29, 1911, p. 151.

New Preserving Medium.—A useful solution for fixing and preserving plants and animals in their natural colors, recently invented by Wickerscheuer, of the Berlin Zoölogic Museum, is prepared by dissolving 100 gms. of alum, 25 gms. of sodium chloride, 12 gms. of potassium nitrate, 60 gms. of potassium carbonate, and 10 gms. of arsenic trioxide in 3000 c.c. of boiling water. To this solution 1200 c.c. of glycerin and 300 c.c. of methyl alcohol are subsequently added. Objects preserved in this liquid are said to retain their form, color, and suppleness to a remarkable degree.—*J. Am. M. Assoc.*, 1911, v. 57, p. 400.

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A NOTE ON THE ASSAY OF FORMALDEHYDE.

By Elias Elvove.

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It has been shown by Williams[1] that the two different types of methods for estimating formaldehyde, namely, those dependent on the oxidation of the formaldehyde and those dependent on its forming condensation products, do not yield concordant results. In explanation of this discrepancy, Williams advances the view that "either the condensation reactions are not complete or a small part of the formic acid is oxidized farther." He also reaches the conclusion that the hydrogen peroxide method is the most satisfactory for strong, impure solutions; while "the potassium cyanide method is recommended for dilute, impure solutions." Recently, the writer has had occasion, in connection with the study of embalming fluids[2] which has been in progress in this laboratory, to make a comparatively large number of determinations of the quantity of free formaldehyde in these fluids. Owing to the possible presence in such fluids of substances other than formaldehyde which on oxidation will yield acids (thus rendering the hydrogen peroxide method inapplicable), or other reducing substances (thus invalidating the iodometric method), it was found necessary to resort to one of the condensation methods, and the potassium cyanide method was chosen. It became of interest, therefore, to look into the points raised by Williams as to the discrepancy of the results obtained by the oxi-

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[1] *Jour. Amer. Chem. Soc.*, **27**, 596–601 (1905).

[2] It is expected that the results of this study will shortly be published as a Hygienic Laboratory Bulletin.

dation and condensation methods and the possible incompleteness of the condensation reactions.

The methods investigated by Williams were those which are most generally recommended for the determination of formaldehyde, namely, the ammonia method of Legler,[3] the hydrogen peroxide method of Blank and Finkenbeiner,[4] and the iodometric and potassium cyanide methods of Romijn.[5] His conclusion that the results obtained by the condensation methods are lower than those obtained by the oxidation methods, is in harmony with the previous work of Smith,[6] who also found that, as compared with the Legler method, "the hydrogen peroxide method almost invariably gave higher results." Smith also seems to hold the view that the potassium cyanide method is applicable to dilute solutions only, since he refers to the KCN method as a "method which is applicable to solutions containing but small quantities of formaldehyde;" and while he concludes that "the iodometric and potassium cyanide methods give good results on dilute solutions," he adds that "it should be remembered that in diluting strong solutions to the range of these methods, a small error in weighing may be considerably multiplied." Apparently influenced by this suggestion of Smith, many authors on analytical chemistry do not recommend the potassium cyanide method except in the case of dilute solutions. Thus Leffmann and Beam,[7] referring to the work of Smith, state that for the determination of formaldehyde the choice of the method "will depend on the strength of the solution," recommending the iodine method of Romijn in the case of moderately strong solutions and the potassium cyanide method for dilute solutions. Likewise, from Schimpf,[8] who also refers to the work of Smith, one gains the information that "the Blank and Finkenbeiner method is very satisfactory for strong solutions" and "the iodometric and potassium cyanide methods give good results on dilute solutions." Similarly, Leach[9] omits the potassium cyanide method as a suitable method for determining formaldehyde in the commercial preservative, although list-

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[3] *Ber.*, **16**, 1333–1337 (1883).
[4] *Ber.*, **31**, 2979–2981 (1898).
[5] *Zeit. anal. Chem.*, **36**, 18–24 (1897).
[6] *Jour. Amer. Chem. Soc.*, **25**, 1028–1035 (1903).
[7] Leffmann and Beam: Food Analysis, 2d ed., p. 84 (1905).
[8] Schimpf: Manual of Volumetric Analysis, 5th ed., pp. 644–645 (1909).
[9] Leach: Food Inspection and Analysis, 2d ed., p. 819 (1907).

ing the iodometric method,[10] the method of Blank and Finkenbeiner and the ammonia method; while the potassium cyanide method he recommends only in the case of very dilute solutions such as are met with when determining formaldehyde in milk.[11] The impression, therefore, which one obtains from the literature on the subject as has been referred to, is that while the potassium cyanide method is admittedly a very good method for determining formaldehyde in dilute solutions it is not recommended in the case of the concentrated or moderately strong solutions, and that in such cases it is preferable to use one of the other methods, of which the hydrogen peroxide method is the most favored. An examination of the leading pharmacopœias as to the methods chosen for assaying commercial formaldehyde solutions also seems to confirm the conclusion that the potassium cyanide method is not generally regarded as a method suitable for use in such cases. Thus the U. S. Pharmacopœia (1905) adopts the hydrogen peroxide method, the German Pharmacopœia (1910) gives the acidimetric sodium sulphite method, the British Pharmaceutical Codex (1907) recommends the ammonium chloride and iodometric methods, while the French Pharmacopœia (1908) agrees with the U. S. Pharmacopœia in giving preference to the hydrogen peroxide method. Finally, we may mention that according to Fresenius and Grünhut[12] there really are only four methods in use for assaying commercial formaldehyde, namely, the ammonia method of Legler, the method in which the

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[10] *Ibid.* It may be noted in this connection that both here and in the first edition (p. 665) there seems to be an error in some of the figures given. For if we take 10 c.c. of a 3 per cent. formaldehyde solution (it is directed that the solution is to be diluted "to a strength not exceeding 3 per cent.") we will be operating on about 0.3 Gm.; and since "two atoms of iodine are equivalent to one molecule of formaldehyde," 0.3 Gm. HCHO will require 200 c.c. of N/10 iodine, whereas according to the given directions only 25 c.c. of N/10 iodine are to be taken. The same error is found also in Leffmann and Beam: Food Analysis, 2d ed., p. 84 (1905).

[11] *Ibid.*, p. 181. There seems to be also an oversight in this connection, since it is directed to use ferric *chloride* as the indicator in titrating the excess of silver.

[12] *Zeit. anal. Chem.*, **44**, p. 13 (1905): "Doch sind es—soweit unsere Kenntnis reicht—im wesentlichen nur vier Verfahren, deren man sich in der Technik zur Betriebskontrolle, sowie zur Wertbestimmung des Handelsproduktes, bedient: die Ammoniak-Methode von Legler, die Oxydation mit Natronlauge in Druckflaschen, die Wasserstoffsuperoxyd-Methode von Blank und Finkenbeiner, und endlich die jodometrische Methode von Romijn."

formaldehyde is treated with sodium hydroxide in pressure bottles, the hydrogen peroxide method of Blank and Finkenbeiner, and the iodometric method of Romijn.

On the other hand, the meaning of the objection advanced by Smith against the use of the potassium cyanide method for determining formaldehyde in strong solutions, namely, "that in diluting strong solutions to the range of these methods, a small error in weighing may be considerably multiplied," is difficult to understand. For supposing that 1 Gm. of the formaldehyde solution is weighed out, diluted with distilled water to 100 c.c. and 25 c.c. of the resulting solution taken for the analysis, and supposing that the delicacy of the balance used is only $\pm$ 0.001 Gm., then the actual amount taken for the analysis would be 0.250 Gm. $\pm$ 0.00025 Gm., involving therefore a possible error of $\pm$ 0.1 per cent. Now if the step of diluting and taking for the analysis an aliquot portion were omitted and the total amount weighed out were used for the analysis, the amount so taken would be 1. $\pm$ 0.001 Gm., the possible error involved would therefore be exactly the same as before, namely, $\pm$ 0.1 per cent. It is possible that "error in weighing" is an oversight, the intention having been—error in *measuring*. If this was the intention, we can readily see how an error might be introduced through an error in measuring. For supposing that instead of using for the analysis the entire amount weighed out, it be diluted to a definite volume and 5 c.c. of this solution taken for the analysis. In measuring out the 5 c.c. there might be an error, say of $\pm$ 0.05 c.c. This would introduce an error of $\pm$ 1 per cent., which would have been avoided if the analysis had been carried out directly on the weighed amount of formaldehyde solution. But even in this case the error would not be "multiplied," unless more than one dilution be made. Moreover, if instead of using only 5 c.c. of the diluted solution a larger volume be taken, say 25 c.c., an equal absolute error in the measuring would, of course, relatively be only one-fifth, or reducing the possible error from $\pm$ 1 to $\pm$ 0.2 per cent. In other words, a procedure which would involve the dilution of a certain weight of the strong formaldehyde solution to 100 c.c. and the use of 25 c.c. of the diluted solution for the analysis, would ordinarily involve no greater error than the inherent errors of volumetric analysis. And since all the methods compared are volumetric, any such errors may be considered equally possible in all of them. For supposing that in measuring out the 25 c.c. of the diluted formalde-

hyde solution there might be an error of ± 0.05 c.c. or ± 0.2 per cent., might there not also be a similar error when the same measuring instrument will be used for measuring out the 25 c.c. of twice normal NaOH (according to Smith) in the case of the hydrogen peroxide method? Besides, in taking 25 c.c. of the 100 c.c. of the diluted formaldehyde solution it is not necessary that the measuring instrument used should measure out exactly 25 c.c. but only that the volume so measured out be one-fourth of the total, and whether this is the case can be readily and conveniently ascertained by using the same measuring instrument for filling the empty 100 c.c. flask with water and seeing whether four fillings will fill it exactly to the mark. This will prove the accuracy of the instrument for this purpose or enable the operator to apply the proper correction. It would seem therefore that if the potassium cyanide method is an excellent method for determining formaldehyde in dilute solutions it may be used with equal advantage in the case of strong solutions by suitably diluting the latter with water.

That such is really the case may be seen from Smith's own results. Using the potassium cyanide method for strong formaldehyde solutions, in which case "all solutions containing more than one per cent. were diluted," the three results given in the case of the 37 per cent. formaldehyde solution are: 37.12, 37.07, and 37.18 per cent. Likewise, the results of Williams, when using the potassium cyanide method for determining the formaldehyde in the concentrated solution, show that very concordant results are obtained by this method. Thus six determinations yielded the following percentages: 35.15, 35.06, 35.23, 35.01, 35.21, 35.07, or a maximum difference from the average (35.12) of only 0.11 per cent. When using the hydrogen peroxide method, four determinations yielded the following percentages: 35.82, 35.92, 35.74 and 35.78, or a maximum difference from the average (35.81) of 0.11 per cent. It is thus seen that the potassium cyanide method can be applied to strong formaldehyde solutions by suitably diluting them, the results thus obtained being equally concordant as those obtained by the hydrogen peroxide method. It therefore remains only to clear up the point as to whether or not the lower results obtained by the potassium cyanide method as compared with those obtained by the hydrogen peroxide method may be due to possible incompleteness of the reaction between the KCN and the formaldehyde.

If we will suppose that the reaction between the KCN and the

formaldehyde is not complete, we must assume that the value of $c_1p_1q_1$ in the general equation

$$V = v - v_1 = cpq - c_1p_1q_1,$$

which is the fundamental equation underlying all chemical dynamics,[13] is not negligible but has a value which would account for the lower results obtained by the KCN method. That is, in the reaction between the formaldehyde and the KCN, which may be represented by the equation

$$CH_2O + KCN \rightleftarrows N \equiv C\text{–}\overset{\displaystyle H}{\underset{\displaystyle H}{\overset{|}{\underset{|}{C}}}}\text{–}O\text{–}K$$

we must assume that the velocity of the reaction which tends to decompose the condensation product back into formaldehyde and KCN has an appreciable value. From the law of mass action it would follow, therefore, that if we were to vary the mass of one of the reacting substances the point at which equilibrium is established should also vary; just as in the classical instance of an incomplete reaction, namely, the reaction between acetic acid and ethyl alcohol, in which case Berthelot and Pean de Saint Gilles[14] found that by varying the amount of alcohol with respect to that of the acid the amount of ester produced also varied, being only 66.5 per cent. of the theory when one equivalent of alcohol was used but increasing to 82.8 per cent. when two equivalents of the alcohol were added. In order, therefore, to determine whether any such variation occurs in the case of the reaction between formaldehyde and KCN, the following experiments were carried out on mixtures of formaldehyde and KCN, in which the amount of KCN added varied from approximately one to three equivalents.

Mode of Procedure.

A formaldehyde solution was prepared by diluting 21.1879 Gms. of a sample of U.S.P. solution of formaldehyde to 2000 c.c. with distilled water. Portions of 15 c.c. of this solution were mixed at room-temperature (22–25° C.) with varying amounts of approximately N/10 KCN, the minimum amount of which was just a little in excess of that theoretically required to combine with all of the formaldehyde taken, while the maximum amount of KCN used was about two equivalents more than necessary for a complete equi-

[13] Jones: Elements of Physical Chemistry, 3rd ed., p. 529 (1907).

[14] *Ibid.* p. 522.

molecular union. The KCN solution was prepared from a sample of Kahlbaum's potassium cyanide, and its value in terms of tenth-normal silver nitrate was determined simultaneously with each series of experiments, the determination being carried out in a manner similar to that used for determining the uncombined cyanide in the experiments. The mixing of the formaldehyde and potassium cyanide solutions was generally effected in Erlenmeyer flasks; and immediately after mixing (the latter operation consuming about half a minute), the resulting solution was added to a mixture of a known amount of silver nitrate and nitric acid in a 200 c.c. measuring flask. The amount of silver nitrate used was sufficient in every case to combine with all of the excess of KCN and calculated to leave in the filtrate, for the subsequent titration, the equivalent of about 2 c.c. of N/10 KCNS per 100 c.c. of the filtrate. The amount of nitric acid used was 10 or 20 c.c. of U.S.P. dilute (10 per cent.) nitric acid. After thoroughly washing the Erlenmeyer flask in which the KCN and formaldehyde solutions were mixed and adding the washings to the flask containing the acidified silver nitrate solution, the whole was made up to 200 c.c. with distilled water, thoroughly shaken, filtered through a dry filter, and 100 c.c. of the filtrate titrated for the excess of silver by means of N/10 KCNS, using 2 c.c. of a 10 per cent. ferric alum solution as indicator. The results obtained are given in Table I.

TABLE I.

EFFECT OF VARYING THE EXCESS OF KCN.

No. of experiment	Amount of formaldehyde solution taken	Amount of N/10 KCN added[a]	Amount of N/10 $AgNO_3$ used	N/10 KCNS required for ½ of filtrate	Found equivalent of the formaldehyde solution in terms of N/10 $AgNO_3$
	(c.c.)	(c.c.)	(c.c.)	(c.c.)	(c.c.)
1	15	19.7	4	1.50	18.45
2	15	20.0	4	1.45	18.65
3	15	21.0	5	1.55	18.84
4	15	22.0	6	1.67	19.07
5	15	23.0	7	1.75	19.21
6	15	24.0	8	1.75	19.20
7	15	25.0	9	1.80	19.29
8	15	27.0	11	1.85	19.36
9	15	30.0	14	1.83	19.29
10	15	40.0	24	1.90	19.30
11	15	50.0	34	1.98	19.34
12	15	60.0	44	2.02	19.29

[a] The KCN solution was only approximately tenth-normal, 48 c.c. being equivalent to 47.4 c.c. N/10 $AgNO_3$.

The results given in Table I show that the maximum result was reached when the excess of KCN was about one-half of an equivalent (exp. 8), while further increasing the amount of KCN up to approximately three equivalents did not appreciably alter the result. The reaction may therefore be regarded as complete, at least for all practical purposes, when the excess of KCN is as much as one-half of an equivalent. On the other hand, when the excess of KCN is less than one-fourth of an equivalent (exps. 1–6), the reaction is incomplete; and when the amount of KCN added is only slightly in excess of that required to combine with all of the formaldehyde present, the result is about 3 or 4 per cent. too low (exps. 1–2). That the excess of KCN must be above a certain minimum in order to insure a complete reaction is not brought out either in the original paper of Romijn or those of Smith or Williams. In fact, none of the literature examined has any reference to this point; while from the statement of Romijn that the method is based on the property [15] of formaldehyde to *immediately* add itself to potassium cyanide and his unmodified general statement [16] that when the KCN is in excess so much of the KCN becomes combined as to correspond to one molecule of KCN for every molecule of formaldehyde, one might suppose that the relative amount of the excess of KCN to be added does not matter. This conclusion would gain further support from the statement of Smith [17] that the determination is carried out by mixing the formaldehyde "with a known quantity of potassium cyanide, the latter being in excess."

In order to determine the effect of varying the time or the temperature, two series of experiments were carried out. In one of these, the mixtures of formaldehyde and KCN were allowed to stand for different intervals of time at the constant temperature of 15° C. and the residual cyanide then determined in the usual way. In the other, the time was constant but the temperature was made to vary between 5° C. and 40° C. In those cases where the mixtures had to stand for a considerable length of time, the flasks containing same were tightly stoppered by means of glass or rubber

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[15] *Zeit. anal. Chem.*, 36, 18 (1897): "die Eigenschaft des Formaldehyds, das Cyankalium sofort zu addiren."

[16] *Ibid.*: "wenn ein Ueberschuss von Cyankalium vorhanden war, wird von dem Cyankalium so viel gebunden, dass auf ein Molecül Formaldehyd ein Molecül Cyankalium kommt."

[17] *Jour. Amer. Chem. Soc.*, 25, 1032 (1903).

stoppers and the value of the KCN solution was controlled by letting it stand under similar conditions and determining its strength at the end of the experiment. The experiments designed to show the effect of temperature were carried out as follows: The formaldehyde solution was placed in one Erlenmeyer flask while the KCN solution which was to be added to it was placed in another similar flask and both were then warmed or cooled to the desired temperature by being set in a large water-bath which was kept about a degree above or below the desired temperature, respectively. The time thus consumed was about half an hour. The KCN solution was then poured into the flask containing the formaldehyde solution and the mixture quickly transferred back again into the flask which contained the KCN solution and mixed in the usual way while the flask containing the solutions was still immersed in the water-bath. This mixture was then quickly poured into a mixture of silver nitrate [18] and nitric acid, in a 200 c.c. measuring flask, and mixed with it. Both flasks were then thoroughly washed with distilled water, the washings added to the silver solution, and the whole made

TABLE II.

EFFECT OF VARYING THE TIME.

Temperature: 15° c.

No. of experiment	Time mixture stood before added to silver solution	Amount of formaldehyde solution taken	Amount of N/10 KCN added [b]	Amount of N/10 $AgNO_3$ used	N/10 KCNS required for ½ of filtrate	Found equivalent of the formaldehyde solution in terms of N/10 $AgNO_3$
	Hours	(c.c.)	(c.c.)	(c.c.)	(c.c.)	(c.c.)
1	0*	25	33	5	1.80	31.33
2	0*	25	40	12	2.30	32.27
3	0*	25	48	20	2.38	32.36
4	1	25	33	5	1.80	31.33
5	1	25	40	12	2.30	32.27
6	1	25	48	20	2.40	32.40
7	18	25	33	5	1.82	31.37
8	18	25	40	12	2.25	32.17
9	18	25	48	20	2.35	32.30
10	42	25	33	5	1.85	31.43
11	42	25	40	12	2.30	32.27
12	42	25	48	20	2.35	32.30

* Added immediately after mixing.

[b] 48 c. c. of the KCN sol. was found equivalent to 47.6 c. c. N/10 $AgNO_3$.

[18] The amount of $AgNO_3$ varied as shown in the tables, while the amount of HNO_3 was the same in all cases, namely, 20 c.c. of 10 per cent. nitric acid.

up to 200 c.c. From this point the procedure was the same as that already described. Each of the different conditions of time and temperature was studied with three different KCN excesses, namely, a KCN excess of approximately one-hundredth, one-fourth, and one-half of an equivalent, respectively. The results obtained are given in Tables II and III.

TABLE III

EFFECT OF VARYING THE TEMPERATURE

No. of experiment	Amount of formaldehyde solution taken	Amount of N/10 KCN added[c]	Amount of N/10 $AgNO_3$ used	N/10 KCNS required for ½ of filtrate	Found equivalent of the formaldehyde solution in terms of N/10 $AgNO_3$
		Temperature: 5°C.			
	(c.c.)	(c.c.)	(c.c.)	(c.c.)	(c.c.)
1	25	33	5	1.90	31.50
2	25	40	12	2.30	32.23
3	25	48	20	2.38	32.32
		Temperature: 15°C.			
4	25	33	15	1.83	31.32
5	25	40	12	2.30	32.18
6	25	48	20	2.40	32.30
		Temperature: 30°C.			
7	25	33	5	1.60	30.86
8	25	40	12	2.20	31.98
9	25	48	20	2.40	32.30
		Temperature: 40°C.			
10	25	33	5	1.35	30.36
11	25	40	12	2.15	31.88
12	25	48	20	2.30	32.10

[c] 48 c.c. of the KCN solution was equivalent to 47.56 c.c. N/10 $AgNO_3$ in exps. 1–3; to 47.5 c.c. N/10 $AgNO_3$ in exps. 4–12.

From the results given in Table II it is seen that when the mixture of KCN and formaldehyde is allowed to stand 42 hours the result obtained is practically the same as when the mixture is immediately added to the silver solution. From the results given in Table III it is seen, however, that a variation in the temperature does have an appreciable effect on the results obtained, especially when the KCN added is only slightly in excess of that required to combine with all of the formaldehyde present. That this is so may also be seen from the following experiments: To each of four Erlenmeyer flasks there were added 25 c.c. of a dilute formaldehyde solution and 33 c.c.

of an approximately N/10 KCN solution and the flasks tightly stoppered by means of rubber stoppers. From the known value of the formaldehyde and KCN solutions [19] the amount of KCN added was calculated to be approximately one-hundredth of an equivalent in excess of that required to combine with all of the formaldehyde present. All these flasks were then set in a large water-bath, the temperature of which was kept at about 40° C., and allowed to remain in this bath for half an hour. At the end of this time, the contents of flask No. 1 was added to a mixture of 5 c.c. N/10 $AgNO_3$ and 20 c.c. of 10 per cent. nitric acid in a 200 c.c. measuring flask and the analysis completed as in the former experiments; while flasks Nos. 2, 3, and 4 were taken out of this bath and set in another large water-bath, which was kept at about 5° C. After remaining in this bath for half an hour, No. 2 was treated as No. 1 while Nos. 3 and 4 were taken out and placed again in the bath at 40° C. After this second warming to 40° C. No. 3 was treated as were Nos. 1 and 2, while No. 4 was taken out of this bath and set again in the bath at 5° C. After this second cooling to 5° C., No. 4 was treated as those preceding it. On titrating half of the final filtrate with N/10 KCNS, the following results were obtained:

								Found equivalent of the 25 c.c. formaldehyde solution in c.c. of N/10 $AgNO_3$
No. 1	required	1.45	c.c.	N/10	KCNS,	corresponding	to	30.59
No. 2	"	2.03	"	"	"	"	"	31.75
No. 3	"	1.48	"	"	"	"	"	30.65
No. 4	"	2.01	"	"	"	"	"	31.71

On now repeating these experiments in exactly the same way except that the excess of KCN was increased [20] to approximately one-half of an equivalent (using 48 c.c. of N/10 KCN, whose factor was 0.9875), the following results were obtained:

								Found equivalent of the 25 c.c. formaldehyde solution in c.c. of N/10 $AgNO_3$
No. 1	required	2.42	c.c.	N/10	KCNS,	corresponding	to	32.24
No. 2	"	2.50	"	"	"	"	"	32.40
No. 3	"	2.35	"	"	"	"	"	32.10
No. 4	"	2.50	"	"	"	"	"	32.40

[19] 25 c.c. of the formaldehyde solution used were found equivalent to 32.4 c.c. N/10 $AgNO_3$, while 33 c.c. of the KCN solution were found equivalent to 32.69 c.c. N/10 $AgNO_3$.

[20] The amount of N/10 $AgNO_3$ used was also increased to 20 c.c.

These results, therefore, like the results given in Table III, show that when only a comparatively small excess of the KCN is used, the effect of a considerable variation in the temperature manifests itself quite markedly in the results; but when the excess of KCN is increased to about one-half of an equivalent, the results obtained at 40° C. are only slightly lower than those obtained at 5° C.; while the results given in Table III show that a variation of the temperature between 5° C. and 30° C. had no appreciable effect on the found value of the formaldehyde solution when the excess of KCN was about one-half of an equivalent. We may conclude, therefore, that the ordinary changes in room-temperature during the year will not appreciably affect the results when the excess of KCN is as much as one-half of an equivalent.

A closer examination of the potassium cyanide method seemed to show also that there is nothing inherent in the basic principle of this method which would prevent its application directly to the concentrated formaldehyde solutions. That such is really the case may be seen from the following experiment: To 0.5505 Gm. of a sample of U.S.P. formaldehyde, weighed out in a closely fitting glass-stoppered Erlenmeyer flask of about 150 c.c. capacity, there were added 100 c.c. of an approximately N/10 KCN solution [21] and the two solutions well mixed. This mixture was then added to a mixture of 35 c.c. N/10 $AgNO_3$ and 20 c.c. 10 per cent. nitric acid in a 200 c.c. measuring flask, the Erlenmeyer well washed and the washings added to the silver solution, the whole made up to 200 c.c., thoroughly shaken, and filtered through a dry filter. 100 c.c. of this filtrate were found to require 2.00 c.c. N/10 KCNS. This would make the formaldehyde in the 0.5505 Gm. of the sample equivalent to 67.75 c.c. N/10 $AgNO_3$ which would correspond to 0.20325 Gm. HCHO or 36.92 per cent. On analyzing a diluted solution of this sample, the result obtained corresponded to 36.98 per cent. It is thus seen that not only is the potassium cyanide method applicable to concentrated formaldehyde solutions by previously diluting them with water but that it may even be applied to the concentrated solution directly, just as in the case of the hydrogen peroxide method.

It has already been pointed out above that in the case of the concentrated formaldehyde solution the H_2O_2 method seems to

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[21] 48 c.c. of this KCN solution was equivalent to 47.4 c.c. N/10 $AgNO_3$.

be the most generally favored and that it is the official method of the present U. S. Pharmacopœia. We may therefore ask, What advantages has the H_2O_2 method over other methods, such as the iodometric or Legler method, which entitle it to this preference? The answer to this may be found partly in the results of Williams [22] who found that in the presence of small amounts of ethyl alcohol, paraldehyde, methyl alcohol, or acetone, the H_2O_2 method gave normal results whereas the results obtained by the iodometric method were abnormal. Similarly, in the case of a formaldehyde solution which contained a small amount of acetaldehyde, the result obtained by the Legler method was 47.8 per cent. instead of 34.87 per cent. in the absence of the acetaldehyde, thus increasing the result in percentage by 12.93; whereas by the H_2O_2 method, under similar conditions, the increase in the percentage was only 2.78 (from 35.82 to 38.6). The results of Williams, however, while showing that the H_2O_2 method is more advantageous than the iodometric or Legler methods, also show that the KCN method is even more reliable than the H_2O_2 method. For not only were the results by the KCN method normal in all cases where the H_2O_2 method gave normal results but even in the presence of acetaldehyde which, as already noted, increased the results by the H_2O_2 method from 35.82 to 38.6 per cent., the result obtained by the KCN method was only slightly higher than in the absence of the acetaldehyde, being 35.12 per cent. in the absence of the acetaldehyde and 35.3 per cent. in its presence; while according to Romijn [23] very exact formaldehyde determinations may be obtained by the KCN method even in the presence of acetaldehyde, acetone or benzaldehyde. We thus see that not only has the KCN method the advantage over the H_2O_2 method in that the reaction on which the former method is based is characteristic for aldehyde but that it may even be used for distinguishing and determining formaldehyde in the presence of certain other aldehydes. The fact also that in the H_2O_2 method the results will be influenced by any substance which on oxidation, under the conditions of the method, will produce acid products capable of consuming a portion of the alkali present, has led Fresenius and

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[22] *Jour. Amer. Chem. Soc.*, 600 (1905).

[23] *Zeit. anal. Chem.*, **23**, 22 (1897): "Die Cyankaliummethode gestattet also auch bei Anwesenheit von Acetaldehyd, beziehungsweise Aceton oder Benzaldehyd, eine sehr genaue Bestimmung des Formaldehyds."

Grünhut[24] to recommend that in assaying commercial formaldehyde by the H_2O_2 method the results obtained should be confirmed by the iodometric method, since it is only when both methods give closely agreeing results that the mean of the two may be taken to represent the actual amount of formaldehyde in the solution.

But these are not the only disadvantages of the H_2O_2 method. For according to Smith,[25] the "working range" of the H_2O_2 method, on the lower end, ends with solutions containing about 5 per cent. HCHO; so that when we have occasion to carry out comparative experiments requiring a knowledge of the formaldehyde content of the strong solutions and also of solutions which contain considerably less than about 5 per cent. formaldehyde, if we would use the H_2O_2 method we would be obliged to use two different methods in the same work. Therefore, should we not prefer a method (the KCN method) which can be universally applied to formaldehyde solutions, whether these be strong or weak with reference to their formaldehyde content, and which is based on a reaction that is characteristic of aldehyde and also permits of distinguishing and estimating formaldehyde in the presence of certain other aldehydes? Finally, we may add that the KCN method has also the advantage of being based ultimately on the beautiful and exact Volhard thiocyanate method and that the silver nitrate solution required comes nearest to the chosen ultimate standard for volumetric solutions—pure metallic silver.[26]

In connection with the study of embalming fluids to which reference has already been made above, it was desired also to obtain

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[24] *Zeit. anal. Chem.*, **44**, 15–16 (1905): "Wir sind immer dafür eingetreten, diese beiden Arbeitsweisen bei der Handelsanalyse, insbesondere bei der Schiedsanalyse, neben einander zu benutzen und das Mittel der nach beiden Verfahren erhaltenen und hinreichend übereinstimmenden Werte als den wahren Formaldehyd gehalt anzusehen. Diese Forderung, zwei verschiedene Methoden anzuwenden, beruht darauf, dass beide nicht eigentlich auf die directe Bestimmung des Formaldehyds abzielen, ihn also nicht in einer wohlcharacterisierten und leicht zu identifizierenden Verbindungsform abscheiden. Beide benutzen viel mehr Reactionen, die ausser dem Formaldehyd noch sehr viele andere Verbindungen zeigen können: die eine lässt alle Substanzen finden, die in alkalischer Lösung durch Wasserstoffsuperoxyd zu Säuren oxydiert werden, die andere alle die jenigen, die in alkalischer Lösung durch Jod oxydiert werden oder in anderer Weise Jod verbrauchen, ohne es beim Ansäuren wieder frei zu geben."

[25] *Jour. Amer. Chem. Soc.*, **25**, 1034 (1903).

[26] Elvove: AMER. JOUR. PHARM., **82**, 203–211 (1910)

an idea as to degree of variation in the strength of the commercial formaldehyde on the American market. Accordingly, samples were obtained from the principal American firms who sell this article. And inasmuch as, for the reasons given above, the KCN method may be considered as more reliable for determining the actual formaldehyde content of such solutions, the determinations were carried out by this method. Seven samples were examined. The results obtained are given in Table IV.

TABLE IV.

SHOWING THE HCHO STRENGTH OF VARIOUS SAMPLES OF COMMERCIAL FORMALDEHYDE.

No. of sample	Amount of formaldehyde[d] solution taken (c. c.)	Amount of N/10 KCN added[e] (c. c.)	Amount of N/10 $AgNO_3$ used (c. c.)	N/10 KCNS required for ½ of filtrate (c. c.)	Found equivalent of the formaldehyde solution in terms of N/10 $AgNO_3$ (c. c.)	Amount of HCHO expressed in percentage by weight (Per cent.)
1	25	48	20	1.75	31.10	35.47
2	25	48	20	2.05	31.74	36.11
3	25	48	20	2.00	31.64	36.21
4	25	48	20	2.30	32.25	36.53
5	25	48	20	2.35	32.34	36.61
6	25	48	20	2.40	32.44	36.98
7	25	48	20	2.91	33.46	37.97

[d] These solutions of formaldehyde contained the following amounts in grams of the respective samples of the concentrated formaldehyde in 2000 c. c.: No. 1, 21.0418; No. 2, 21.0958; No. 3, 20.9690; No. 4, 21.1879; No. 5, 21.2005; No. 6, 21.0512; No. 7, 21.1459.

[e] The found value of the KCN solution was as follows: In the case of No. 1, 48 c. c. was equivalent to 47.6 c. c. N/10 $AgNO_3$; in No. 4, to 47.65; and in the remainder, to 47.64 c. c. N/10 $AgNO_3$.

The results given in Table IV show that the majority of the samples examined contained slightly less formaldehyde than is required by the present U.S.P. ("not less than 37 per cent. by weight"), and that only two (Nos. 6 and 7) of the seven samples examined may be said to have come up to its requirement. Similar results have also been obtained by Evans Sons Lescher and Webb,[27] who found that the nine samples of commercial formaldehyde solution which they examined ranged from 37 down to 35.4 per cent.

[27] Evans Sons Lescher and Webb: Analytical Notes, 1907, 1908, p. 22.

of absolute formaldehyde by weight. Likewise, Bachman [28] reports solution of formaldehyde ranging from 36.6 per cent. to 31.8 per cent., instead of the minimum of 37 per cent. as required by the present U.S.P. Finally, we may mention in this connection that the formaldehyde requirement of the French Pharmacopœia (1908) and also of the German Pharmacopœia (1910) is only 35 per cent. by weight of absolute formaldehyde. On the other hand, with the exception of only one sample (No. 1), all contained more than 36 per cent. by weight of absolute formaldehyde. Therefore, bearing in mind the comparative difficulty of manufacturing and keeping unaltered solutions of formaldehyde of considerably higher concentration than the minimum of the present U.S.P.; and also that by making the U.S.P. requirement more in harmony with these latter pharmacopœias and with what seems to be the actual condition of the American market, it would not mean that the purity requirement will be lowered but only that the solution will be just a little less concentrated; it would seem advisable that the formaldehyde requirement, in the next revision of the U.S.P., be changed from the present minimum of 37 per cent. to a minimum of 36 per cent. by weight of absolute formaldehyde. Also that the KCN method might with advantage be substituted for the present H_2O_2 method. The KCN method, applied to U.S.P. solution of formaldehyde, may be carried out as follows:

Transfer 0.5 c.c. of the sample of Solution of Formaldehyde to a well-stoppered Erlenmeyer flask of about 150 c.c. capacity and determine its weight. Add to it immediately 100 c.c. of a solution of potassium cyanide of a strength close to tenth-normal (6.5 Gm. KCN to 1000 c.c.), the exact strength of which is known. Mix well, and add to a mixture of 40 c.c. N/10 silver nitrate and 10 c.c. of dilute (10 per cent.) nitric acid, in a 200 c.c. measuring flask. Wash the Erlenmeyer flask, adding the washings to the silver solution, and make up the whole to 200 c.c. Shake thoroughly, filter through a dry filter, and titrate the excess of silver in 100 c.c. of the filtrate by means of N/10 ammonium or potassium sulphocyanate, using ferric alum as indicator. The number of c.c. of N/10 sulphocyanate found to require, multiplied by 2, and the product subtracted from 40, will give the equivalent of the uncombined KCN in c.c. of

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[28] Proc. Minnesota Pharm. Ass., 1907, p. 41; from Bull. No. 63, Hyg. Lab., U. S. Pub. Health & Mar. Hosp. Serv., Wash., p. 295.

N/10 $AgNO_3$. Subtracting this from the corresponding equivalent of the total KCN added, multiplying the difference by 0.3, and dividing this product by the weight of the sample taken, the quotient will represent the percentage by weight of absolute formaldehyde in the sample.

TINCTURE OF CANTHARIDES.[1]

By E. G. Eberhardt, Indianapolis, Ind.

About two years ago when an attempt was made to prepare a standardized fluid extract of cantharides, it was discovered that such a preparation was an impossibility because of the sparing solubility of cantharidin in alcohol, the latter being considered the only proper solvent. When the investigation was extended to the tincture it was found that, for the same reason, a tincture could not be made which represented 10 per cent. of drug. The latter, if of good quality, will average about 1 per cent. of cantharidin, but the tincture made by the official method only assays from 0.03 per cent. to 0.04 per cent. This same fact was brought out in a paper on "Tincture Cantharides," by Prof. W. L. Scoville, read at the 1910 meeting of the American Pharmaceutical Association and he there recommends a menstruum of alcohol 15 volumes and glacial acetic acid 1 volume as giving a much better tincture, the results averaging from 0.057 per cent. to 0.064 per cent. Prof. Scoville also determined the solubility of cantharidin in official alcohol at 25° C. to be 1 : 1333 (W.V.). Accordingly it would be possible to have a tincture made with alcohol assaying .075 per cent. unless the accompanying extractive would decrease the solvent power of the menstruum for cantharidin.

As complete extraction of cantharides could not be accomplished with alcohol at the ordinary temperature an attempt was made to obtain an alcoholic preparation of maximum strength by the use of heat. A lot of tincture was made by digesting the drug in a closed vessel with hot alcohol for about two hours, allowing to cool at room temperature, draining off the liquid, digesting the residue with a fresh portion of alcohol and washing the residue finally with sufficient alcohol to make the required amount. This

[1] Presented before the Division of Pharmaceutical Chemistry at the Indianapolis meeting of the American Chemical Society, July, 1911.

tincture assayed 0.031. Hot percolation was employed on another lot, stopping when the correct amount of tincture was obtained. This assayed 0.035. The drug was thereupon further percolated, the weak percolate reduced to small volume under reduced pressure and incorporated with the first percolate which then assayed 0.0499. The small amount of light-colored sediment which forms in these tinctures, on standing, contains cantharidin which may be ammonium cantharidate or some similar combination, as it is quite likely that ammonia or an amine is formed when the drug is subjected to heat or by aging. A small experimental lot was now made, using hot percolation and obtaining four successive fractions each equal in volume to the amount of tincture to be finished. These assayed as follows:

No. 1—.058	No. 3—.003
No. 2—.010	No. 4—.002

It is evident that the first two fractions contain practically all the cantharidin that can be obtained in this way. This, however, is only about two-thirds of what was in the drug and the question arises, why were the succeeding fractions so weak? The solution probably lies in the condition indicated above, that part of the cantharidin is present as a cantharidate which is but very sparingly soluble in alcohol. From this, it seems imperative that some acid be used if alcohol is to be the extracting agent or if, as later results show to be desirable, the cantharidin is wanted in the uncombined state. However, a better solvent than alcohol is needed to make a full-strength tincture even though acid is used. This is shown by the fact that when the drug was moistened with a mixture of equal parts glacial acetic acid and alcohol, allowed to stand several hours and then percolated with alcohol, the resulting tincture assayed only .04.

The plan of converting all the cantharidin into cantharidate was next tried and a portion of drug was mixed with magnesium oxide, moistened with water and dried at a gentle heat. It was then divided, one-half being percolated with alcohol and the other half with dilute alcohol. The resulting tinctures assayed: alcohol .023 and dilute alcohol 0.053, showing that the weaker menstruum is much the better for combined cantharidin. Using a caustic alkali, it was found necessary to add considerable excess as the fat present in the drug requires a certain amount for saponification. A quantity of drug was moistened with one-tenth its weight of caustic

potash dissolved in water, the magma heated on the water-bath to complete the reaction and, as it was in no condition to percolate, it was dried at a gentle heat and ground. It could then be percolated with dilute alcohol and yielded a tincture assaying 0.106, which practically represented the full strength of the drug.

This tincture was compared for vesicating power with a U.S.P. tincture assaying about one-third as much cantharidin. Three drops of the U.S.P. tincture caused distinct redness on a man's arm and six drops produced vesication. Three drops of the alkaline tincture produced no visible effect and six drops only a slight redness. When equal volumes were evaporated spontaneously, a few drops of acetic acid added to each, and then mixed with a definite amount of lead plaster, the effects were about equal when applied to a shaven area on a dog's leg, each producing redness in five hours, and vesicles in 15 hours. As the presence of lead plaster may have prevented to a considerable extent the liberation of cantharidin, this test was repeated, using lanolin as a base. The result did not materially differ from that previously obtained even when the test was repeated with a larger amount of acetic acid. When the tincture itself was acidified and filtered it assayed only .062, showing a loss of 40 per cent. of cantharidin which in all probability would be still greater on longer standing. As acetone is a much better solvent for cantharidin than alcohol a tincture was made by exhausting the drug with acetone, recovering the solvent and dissolving the residue in alcohol. This tincture assayed 0.066 and probably contained all the free cantharidin in the drug. It is a question, however, whether this amount of cantharidin would remain permanently in solution in an alcoholic tincture and as there can be no serious objection to the use of acetone as a menstruum, a final experiment was made in which the cantharides was moistened with a mixture of acetone 19 parts and glacial acetic acid 1 part, and then percolated with acetone. When one-half the required amount of tincture had been obtained, the percolate was almost colorless and therefore this first half was assayed separately from the second half. A second fraction equal in volume to the finished tincture was also obtained and assayed. The results were as follows:

$$\left.\begin{array}{l}\text{1st half of tincture} = 0.140 \\ \text{2d half of tincture} = 0.0078\end{array}\right\} \quad \text{average} = 0.0739$$

Fraction No. 2 = 0.01

The finished tincture, that is the mixture of the two halves, was found to be more actively vesicant than the U.S.P. tincture.

It is probable that the acid added to the first part of the menstruum was insufficient in amount, or that, for some other reason, some of the combined cantharidin failed to be liberated. This point should have further investigation. But it is very evident from the way in which extraction proceeded that acetone is a much better solvent for extracting cantharides than alcohol, and if used there would be practically no difficulty in making a full strength tincture. Some suitable acid should, however, be added to that part of the menstruum used for moistening and macerating the drug in such proportion as to insure the liberation of all combined cantharidin.

To summarize, cantharides can be exhausted by gently heating with a solution of a caustic alkali to convert the cantharidin into cantharidate, drying, grinding and extracting with dilute alcohol. The resulting preparation, however, is weak in vesicating power. Exhaustion can also be accomplished by liberating any combined cantharidin present in the drug by means of a suitable acid and then extracting with acetone. The resulting preparation is actively vesicant.

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THE ASH CONTENT OF DRUGS.[1]

By M. I. Wilbert, Washington, D. C.

In recent years there has been evidenced a growing disposition to place considerable reliance on the ash content of drugs as an aid in determining the nature and purity of the product under examination.

With a view of ascertaining what if any uniformity exists in the permissible ash content of official drugs, an analysis of the requirements made in ten of the recently published pharmacopœias was made and the maximum ash content of some of the more widely used drugs is herewith presented in the form of a table.

Restricting the permissible quantity of ash in connection with vegetable or crude drugs is a comparatively modern requirement. It was introduced in the second edition of the German Pharmacopœia,

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[1] Read at the Boston meeting of the American Pharmaceutical Association, August, 1911.

published in 1882, and also appears in connection with a limited number of the drugs described in the U.S.P. of the same period. The number of official limitations for ash was increased but slowly and in the German Pharmacopœia for 1900 we find but 12 while in the corresponding U.S.P. VIII there are 15 such requirements in connection with the monographs for crude drugs.

The Netherlands Pharmacopœia published in 1905 appears to have been the first of the more widely known pharmacopœias to include an appreciable number of ash determinations, a total of 41.

In the Ph. Austr. VIII, published in 1906, this number is increased to 147, the maximum up to the present time, though the aggregate of the Ph. Helv. IV is nearly if not quite as great.

The Ph. Svec. IX, published in 1908, contains but a comparatively few definite figures, and the Ph. Hung. III, published in 1909, despite the fact that it follows the Austrian Pharmacopœia in many of the official requirements includes but a limited number of limitations for ash.

The German Pharmacopœia, which for some decades appears to have served as a model for the elaboration of our own U.S.P., has been continued within conservative lines and the new D.A.B.V. published in 1910 contains but a total of 34 requirements for ash content.

The impracticability of deducing any definite generalizations from the permissible limitations for ash included in the several pharmacopœias is well illustrated by the appended table. For many of the drugs the figures vary from 10 to 100 per cent. and in the limited number of cases where there is little or no variation, lupulin, for instance, the figures given have been found to be altogether too low for the commercially available product.

The variation in the actual ash content of drugs necessarily depends on many factors that are entirely beyond the control of the pharmacist or the dealer in drugs, but the frequently observed variation in the ash content of the same sample or lot of a drug is due to causes that are deserving of careful consideration on the part of the revisers of the Pharmacopœia. The fundamentally important factors for securing uniformity are to be sought in the method of incineration and the method of sampling employed therewith.

In the routine work of the ordinary analytical laboratory it is impracticable to incinerate more than 1 or 2 Gms. of a sample of crude drug, and it is quite apparent that it would be difficult indeed

to secure a representative sample of a root, bark, leaf or herb that could be relied upon without resorting to comminution and subsequent mixing of an appreciable quantity of the drug.

This difficulty of securing representative samples of many crude drugs has no doubt deterred the revisers of some of the more recent pharmacopœias from adopting the ash content factor more freely.

It is generally agreed that the exact method for determining the residual ash should be described so as to obviate, if possible, the likelihood of the residue retaining an undue amount of unconsumed carbon.

The Ph. Austr. VIII, despite the fact that it includes upwards of 150 limitations for the ash content of drugs, does not provide a method for determining this rather important requirement, and the several critics of this Pharmacopœia have not failed to assert that the commission in charge of the revision adopted theoretic rather than practical standards for many of the pharmacopœial drugs.

The Ph. Helv. IV directs that ash determinations are to be made by heating from 1 to 2 Gms. of the substance at first moderately, with a low flame, and then gradually increasing the temperature until the residual ash is free from carbon.

The nature of the container in which the substance is to be incinerated is not specified and no provisions are made for aiding the combustion of protected carbon particles.

The new German Pharmacopœia process is much more complete. It directs that a suitable quantity of the substance is to be incinerated in a recently heated and tared crucible, and in the event that complete combustion of the carbon particles is not brought about by continued moderate heating the material is to be leached out with hot water and the residual carbon again heated as before. The resulting solution is subsequently evaporated and the weight of the dry residue is added to that of the ash.

This Ph. Germ. V method has been liberally criticised, many pharmacists believing that the leaching out method is much more time-consuming than the methods which involve the use of clean sand for distributing the particles of carbon and the use of oxygen carriers such as nitric and oxalic acids for facilitating combustion.

Considerable difference of opinion appears to exist regarding the desirability of determining the ash, and other analytical factors, on the air-dried drug or on the drug dried to constant weight in an exsiccator.

In view of the fact that it is the air-dry drug that appears in commerce and is generally used in the making of galenical preparations as well as dispensing it would appear preferable to base phar-

TABLE SHOWING THE MAXIMUM ASH CONTENT OF SOME WELL KNOWN DRUGS INCLUDED IN 10 OF THE RECENTLY PUBLISHED PHARMACOPŒIAS.

Title of Drug.	Ph. Germ. V.	Ph. Hung. III.	Ph. Ital. III.	Ph. Fr. V.	Ph. Svec. IX.	Ph. Helv. IV.	Ph. Aust. VIII.	Ph. Belg. III.	Ph. Ndl. IV.	U. S. P. VIII.
Acacia	5.0	5.0	4.0	...	5.0	4.0	3.0	5.0	4.0	4.0
Adeps lanæ	0.1	0.05	...	...	...	...	...	0.05	0.10	0.30
Aloe	1.5	...	2.0	1.5	...	1.0	1.0	...	1.5	...
Althaea	...	...	...	...	...	6.0	6.0	7.5	7.0	...
Amylum	1.0	0.5	1.0	1.0	...	0.5	0.5	1.0	1.0	...
Anisum	10.0	...	...	...	...	10.0	10.0	12.0	...	...
Asafœtida	15.0	...	10.0	10.0	10.0	20.0	10.0	10.0	10.0	15.0
Belladonna folia	15.0	...	...	...	...	15.0	15.0	...	...	...
Benzoimum	2.0	...	2.0	2.0	...	1.5	2.0	...	2.0	2.0
Calumba	...	...	...	...	...	8.0	6.0	...	...	...
Cantharis	8.0	...	7.0	...	...	8.0	8.0	...	9.0	8.0
Capsicum	6.5	5.0	...	...	...	6.5	6.5	...	...	...
Carbo ligni	5.0	...	2.0	...	...	2.0	...	...	2.0	...
Cardamomum	...	...	...	...	...	10.0	8.0	...	8.0	4.0
Carum	8.0	...	...	...	...	8.0	7.0	...	...	8.0
Caryphyllus	8.0	...	...	...	...	7.0	8.0	...	6.0	8.0
Cinchona	...	...	6.0	...	...	6.0	6.0	...	8.0	...
Cinnamomum zeylanicum	5.0	...	...	...	...	5.0	5.0	7.0	8.0	4.0
Coccus	...	...	...	...	...	6.0	...	...	...	6.0
Cubeba	8.0	...	9.0	...	...	8.0	9.0	...	10.0	...
Digitalis	...	...	...	...	...	10.0	10.0	12.0	...	...
Ergota	...	...	5.0	...	...	5.0	5.0	...	5.0	...
Fœniculum	10.0	...	...	...	...	10.0	10.0	12.0	...	...
Gelatina	2.0	...	2.0	2.0	...	2.0	2.0	2.0	3.0	...
Gentiana	...	...	...	...	...	6.0	5.0	7.0	6.0	...
Glycyrrhiza	...	...	...	...	...	6.0	6.0	7.5	6.0	...
Gossypium purificatum	0.3	...	0.3	0.4	...	0.5	0.5	0.3	0.3	0.3
Granatum	...	...	...	...	...	15.5	10.0	...	15.0	...
Hydrastis	...	...	6.0	...	...	6.0	6.0	...	6.0	...
Hyoscyamus	24.0	...	...	...	...	...	...	...	...	...
Ipecacuanha	...	...	4.0	...	...	4.0	5.0	...	6.0	...
Jalapa	6.5	...	4.5	...	...	6.5	5.0	...	...	...
Linum	5.0	...	6.0	...	...	5.0	5.0	...	...	...
Lupulinum	...	...	10.0	...	...	10.0	10.0	...	...	10.0
Lycopodium	3.0	...	4.0	...	...	3.0	3.0	4.0	5.0	5.0
Manna	3.0	...	3.5	...	4.0	3.0	4.0	...	...	...
Mel	0.8	...	0.4	...	0.5	0.8	0.4	0.5	...	0.3
Myrrha	7.0	...	6.0	...	6.0	6.0	6.0	6.0	5.0	...
Nux vomica	3.0	...	...	...	...	3.5	3.0	...	...	...
Opium	...	...	6.0	...	...	5.0	6.0	...	...	...
Rhamnus purshiana	6.0	...	...	...	...	...	...	...	10.0	...
Rheum	12.0	...	12.0	...	...	13.0	12.0	...	12.0	...
Saccharum	0.1	...	...	0.075	...	...	...	...	0.1	...
Saccharum lactis	0.25	...	...	...	...	0.2	...	...	0.1	0.25
Scilla	5.0	...	...	...	...	5.0	8.0	...	...	...
Senna	12.0	...	...	...	...	12.0	10.0	12.0	8.0	...
Sinapis	...	...	5.0	...	...	5.0	5.0	5.0	8.0	...
Stramonium	20.0	...	...	...	...	...	...	...	...	...
Valeriana	...	...	...	...	...	12.0	10.0	15.0	...	...
Zingiber	7.0	...	...	...	...	7.0	5.0	...	8.0	...

macopœial requirements on the commercial drug and to add such other restrictions as may be found necessary to limit the percentage of contained moisture.

This is apparently the view taken by the revisers of the German Pharmacopœia as that authority now requires that the official tests are to be applied to the air-dried substances unless otherwise directed.

From the available evidence it would appear that the determination of the ash content of official drugs is practicable and important in connection with non-structural drugs, like gums and resins, pollen grains, seeds, spices and powdered drugs generally.

It is not generally applicable to leaf drugs, barks or roots in the uncomminuted form because of the difficulty of sampling.

To insure correlating results the method to be employed must be described, and, other things being equal, this method should be one that can be easily followed by retail druggists ordinarily well equipped for work of this kind.

EXPERIMENTS WITH THE CAT METHOD FOR TESTING DIGITALIS AND ITS ALLIES.

By C. R. Eckler.

There are at present four American methods in use for the physiological testing of the digitalis series, namely: The twelve-hour frog method, proposed by Houghton; the one-hour frog heart method, proposed by Famulener and Lyons; the guinea pig method, proposed by Reed and Vanderkleed; and the cat method, proposed by Hatcher and Brody.

In view of the large amount of work which is being carried out just now with these methods, with the hope that some one may be found sufficiently accurate and convenient to justify its insertion into the next Pharmacopœia, it seemed proper to report some results obtained with one of these—the cat method of Hatcher and Brody. They describe their method in the American Journal of Pharmacy for August, 1910, and state that it is an accurate one, and one that can be conveniently carried out by the retail pharmacist. The purpose of this study was to ascertain with what ease the method could be used, and what uniformity of results could be obtained. Since they have not given all the details of manipulation, I will describe the method as I used it, my endeavor being to carry it out in all respects just as they did.

Fully grown apparently healthy cats were selected. In general these were stray cats of the city, and represented all common breeds and mixtures. They were accurately weighed, and then anæsthetized in the following manner: The animal was placed in a small box, just large enough to accommodate the body, with a small circular notch at the top of one end of a size which would just admit the neck. A cat in the box with the neck in place, the sliding lid was forced shut and held by a peg. Thus the animal was unable to withdraw its head. The anæsthetic was then given from a small copper cone carrying on a transverse screen a pad of cotton or gauze. A few drops of chloroform were placed on the cotton at the start in order to hasten this operation. As soon as the animal was unconscious this pad of cotton was replaced by another upon which only ether was dropped. The cat was then tied on an animal board (somewhat resembling the Harvard) with back down, legs outstretched, and head securely fastened in a holder. This board, supported on legs, was made so as to drain at a point near the lower (tail) end, under which a receiving vessel was placed. The animal in place, the femoral veins were dissected out and small glass cannulæ inserted. The solutions were contained in burettes, the ouabain in one and the digitalis body in the other, and were conveyed to the cannulæ by narrow catheter tubing. The injection extended, as near as could be arranged, over a period of ninety minutes.

The Ouabain Solution.

Merck's crystalline ouabain was used. The weighing was done on an accurate chemical balance, and a stock solution 1:10,000 was made in a one litre volumetric flask. For use, samples were drawn off with a pipette and diluted to the strength 1:100,000 in a narrow glass-stoppered 200 c.c. cylinder. All dilutions were made with recently prepared physiological salt solution. (0.75 per cent. NaCl.) The stock solution was kept in a cool dark cupboard, and in no case was used after two weeks old. The solution for use was made up as needed.

After running two preliminary experiments to become acquainted with the technic, a series of twenty-six experiments with ouabain was begun. The procedure and results were as follows:

The weight of the animal having been taken, the theoretical amount of solution required was calculated. Since the lethal dose

of ouabain for cats, according to Dr. Hatcher, is .0001 gramme per kilogramme of body weight, the theoretical amount of solution would be the number of cubic centimeters required, for any given animal, to supply .0001 Gm. per Kgm. And since each cubic centimeter of a 1 : 100,000 solution would contain .000.01 Gm., a 3.2 Kgm. cat, for example, would require 32 c.c. Ninety minutes being the period of injection, the proportionate part of the theoretical amount necessary to be run in each minute or two minutes, was calculated. The operator seated at the table, continued the anæsthesia by placing a small pad of gauze over the nose and supplying only sufficient ether to just keep the animal quiet. The burette having been filled and the time noted, the injection was begun, running in slowly every minute or two minutes the amount proportioned. The cat was carefully watched, particularly toward the end when the larger part of the theoretical amount had been injected. Death was usually preceded by very rapid respiration and decided convulsive movements, after which the respiration ceased to be regular and was prolonged for a few minutes only by gasps. As soon as these symptoms of approaching death appeared, the injection was stopped. If after waiting a few minutes the animal did not die, the injection was continued very slowly and with great caution. When respiration had ceased to be regular, the number of cubic centimeters of solution used and the time were noted, and before the gasping had entirely ceased the heart was exposed. In the majority of cases, rhythmic contractions of the heart had ceased. Sometimes the heart was in feeble delirium, but usually the left ventricle was still and the other chambers were feebly contracting. Out of twenty-six experiments with ouabain, sixteen with strophanthus, and twenty-seven with digitalis, only seven hearts were found beating rhythmically, and in these the contractions were very feeble. Twelve hearts showed the left ventricle in quite complete systole. It should be remembered that regular respiration had ceased from one to three minutes previous to the exposure of these hearts. In one instance under ouabain, paraldehyde was used as the anæsthetic. (1.8 c.c. per Kgm. Merck's.) Immediately upon appearance of the gasping, without opening the thorax, artificial respiration was instituted. The heart seemed to improve, and continued to beat until at the end of ten minutes one cubic centimeter more of the solution was slowly injected when it stopped. With cat No. 26 artificial respiration was supplied all through the experiment, still the animal died within the ninety

minutes, having received almost the exact theoretical amount. To accurately determine the effect of artificial respiration upon the lethal dose would of course require a large number of experiments, an interesting point, but one I have not been able to work out for lack of time and animals.

OUABAIN.

Date	Cat No.	Sex	Wt. in Kgms.	c.c. Sol.	Ouabain in Gms. per Kgm.	Time in Min.
12–16–10	1	Male	2.10	25.0	.000,119	99
12–18–10	2	Male	4.70	32.0	.000,068	70
12–21–10	3	Male	2.80	25.0	.000,089	71
12–22–10	4[1]	Male	2.00	15.0	.000,075	75
12–24–10	5	Female	1.10	11.5	.000,104	118
12–24–10	6	Male	1.80	16.8	.000,093	87
1– 4–11	7	Male	1.70	16.0	.000,094	93
1– 5–11	8	Male	2.70	16.0	.000,060	61
1–30–11	9	Female	1.19	11.2	.000,094	88
1–31–11	10	Male	2.11	22.1	.000,105	94
2– 1–11	11	Female	1.77	17.4	.000,098	95
2– 2–11	12	Female	2.33	19.6	.000,084	82
2– 2–11	13	Female	0.97	13.0	.000,134	104
2– 3–11	14	Female	2.13	27.0	.000,126	106
2– 4–11	15	Male	3.42	46.0	.000,134	106
2– 4–11	16	Female	2.43	26.5	.000,109	97
2–10–11	17	Male	2.50	23.0	.000,092	82
2–11–11	18	Male	3.27	32.7	.000,100	91
2–13–11	19	Male	2.94	25.5	.000,086	77
2–13–11	20	Male	1.81	17.5	.000,096	86
2–14–11	21	Male	2.40	20.0	.000,083	76
2–14–11	22	Female	1.87	16.0	.000,085	83
2–15–11	23	Male	2.28	22.0	.000,096	90
2–15–11	24	Female	2.25	21.0	.000,093	87
2–15–11	25	Female	1.92	13.5	.000,070	65
6–14–11	26	Female	2.38	24.0	.000,100	87

[1] Received paraldehyde instead of ether.

Two samples of strophanthus seed (Kombe) were received for testing at this time. These were reduced to No. 60 powder. Ten gram samples were placed in 150 c.c. Erlenmeyer flasks, supplied with good, tightly fitting corks, and macerated with 40 c.c. of 75 per cent. alcohol for 72 hours with occasional agitation. The content of each flask was then poured into a small narrow percolator fitted at the neck with a tight pluget of cotton. The first portion of each percolate was returned and the percolation was then allowed to pro-

ceed at the rate of 10 drops per minute. Seventy-five per cent. alcohol was added from time to time until 200 c.c. of percolate were obtained, thus finishing a 5 per cent. tincture. For injection, 1 : 6000 solutions were used. These were made in the same manner as described under ouabain. The results from eight experiments on each of these samples were as follows:

STROPHANTHUS SEED NO. B-565.

Dilution 1:6000 — 1 c.c. = .000,166 gm. drug.

Date	Cat No.	Sex	Wt. in Kgms.	c.c. Sol.	Strophanthus in Gm.	Time
2-16-11	1	Male	2.23	16.0	.001,19	69
2-16-11	2	Male	2.65	22.0	.001,37	100
2-16-11	3	Female	2.82	26.0	.001,53	98
2-17-11	4	Male	2.29	22.9	.001,66	107
2-17-11	5	Male	2.11	24.0	.001,88	100
2-18-11	6	Male	2.98	30.0	.001,66	95
2-18-11	7	Male	3.07	31.0	.001,67	100
2-18-11	8	Female	2.04	18.0	.001,46	66

STROPHANTHUS SEED NO. B-566.

2-21-11	1	Male	2.45	26.4	.001,78	102
2-21-11	2	Male	3.17	23.0	.001,20	60
2-21-11	3	Male	1.29	11.1	.001,42	71
2-22-11	4	Male	3.00	24.0	.001,32	60
2-22-11	5	Male	3.17	25.5	.001,33	87
2-22-11	6	Female	3.14	23.5	.001,23	87
2-23-11	7	Male	3.82	29.0	.001,24	95
2-23-11	8	Male	2.93	25.0	.001,41	111

Hatcher and Brody have found after many experiments that if digitalis and the other members of the series are injected, like ouabain and strophanthus, until the animal dies, the results will usually be too high—necessitating a correction of about 20 per cent. They have therefore devised a modification of the method which gives results comparable in accuracy, they believe, to those obtained with crystalline ouabain itself. This modification is as follows:

A measured quantity of the digitalis solution (I understand about 50 per cent. of the required amount) is injected during the first period of about ten minutes. After an interval of about twenty minutes the injection is continued, substituting ouabain solution for the digitalis, until the animal dies. The difference between the

amount of ouabain actually used to complete the experiment, and the theoretical amount necessary to kill the animal in the absence of the digitalis body, represents the amount of ouabain to which the digitalis body used is equivalent. The amount of digitalis body equivalent to .0001 Gm. or one "cat unit," is then calculated.

EXAMPLE TO SHOW METHOD OF CALCULATION.

Digitalis solution = 1 : 100 — 1 c.c. = .010 Gm.
Ouabain solution = 1 : 100,000 — 1 c.c. = .000,01 Gm.

Cat weighing 3.21 Kgms. received { 30.2 c.c. digitalis sol. (.302 Gm. drug) or, .0940 Gm. drug per Kgm. body weight; 5.5 c.c. ouabain sol. (.000,055 Gm. ouabain) or, .000,017 Gm. ouabain per Kgm. of cat.

The difference between .000,017 Gm., the amount of ouabain (per Kgm.) actually used to complete the experiment, and .000,100 Gm., the theoretical amount, or one "cat unit," which would have been required in the absence of the digitalis body, is .000,083 Gm.

.094 Gm. of the digitalis is therefore equivalent to .000,083 Gm. ouabain, or .094 Gm. of the digitalis = 83 per cent. of one "cat unit."

.113 Gm. of the digitalis would then be equivalent to one "cat unit."

F. E. DIGITALIS.

No. 405467.

Digitalis dilution 1:100
Ouabain dilution 1:100,000

Date	Cat No.	Sex	Wt. in Kgms.	c.c. Dig. Sol.	c.c. Ouabain Sol.	Equiv. in Gm. of 1 Cat Unit	Time in Min.
2-27-11	1	Female	3.21	30.2	5.5	.113,5	95
2-27-11	2	Male	2.88	25.0	3.0	.096,8	61
2-27-11	3	Male	2.87	25.0	7.0	.115,2	100

F. E. DIGITALIS.

No. 416233.

5- 8-11	1	Male	2.33	14.0	5.2	.077,3	66
5- 8-11	2	Female	2.18	12.0	3.6	.065,8	65
5- 9-11	3	Male	2.07	11.0	4.6	.068,2	80
5- 9-11	4	Female	1.83	10.0	6.7	.086,1	73
5-10-11	5	Male	2.21	11.1	6.0	.068,8	97
5-10-11	6	Male	2.40	14.0	8.0	.087,4	82

F. E. Digitalis.

No. 335929.

5-11-11	1	Female	1.72	10.0	3.5	.072,8	79
5-11-11	2	Male	3.18	15.0	21.0	.138,7	114
5-11-11	3	Female	1.75	11.7	9.0	.137,5	100
5-12-11	4	Female	1.89	10.0	10.0	.112,3	90
5-13-11	5	Female [1]	2.15	10.0	15.0	.153,4	155
5-15-11	6	Female [1]	2.55	12.0	25.5	.522,7	114
5-15-11	7	Female [1]	1.82	12.0	12.0	.193,5	80
5-16-11	8	Male	3.00	16.0	17.5	.127,9	115
5-17-11	9	Female [1]	2.90	17.5	9.7	.090,6	75
5-18-11	10	Male	2.46	16.0	7.0	.090,8	75
5-18-11	11	Female	1.98	11.0	8.0	.093,2	85

[1] In varying stages of lactation.

Tr. Digitalis No. 2-B.

5-22-11	1	Female	2.11	13.0	3.5	.073,2	61
5-23-11	2	Male	2.89	14.0	16.5	.112,6	95
5-23-11	3	Female [1]	2.35	13.0	15.0	.154,2	85
5-24-11	4	Male	2.83	17.0	3.0	.067,1	111
5-24-11	5	Female [2]	2.46	15.0	14.0	.141,4	106
5-24-11	6	Male	2.30	16.4	8.0	.109,3	81
5-25-11	7	Female	3.00	16.0	7.5	.071,1	73

[1] Lactating.
[2] Apparently in period immediately following lactation. Glands were still enlarged, but not functuating.

Assays on Foregoing Preparations by Other Methods.

One-Hour Frog Heart Method. Variety Rana Pipiens. Temperature 20° C.

Strophanthus Seed B-565.

Weight of frog in Grammes	Dose per Gramme	Result
36.5	.000,006,0	Stopped
40.8	.000,005,0	"
15.1	.000,005,0	"
28.1	.000,004,0	"
39.6	.000,004,0	"
23.0	.000,004,0	"
43.8	.000,003,5	"
36.4	.000,003,5	"
48.7	.000,003,5	Beating
35.2	.000,003,0	"
19.4	.000,003,0	"

STROPHANTHUS SEED B-566.

18.2	.000,006,0	Stopped
20.6	.000,005,0	"
23.6	.000,005,0	"
15.4	.000,005,0	"
43.7	.000,005,0	"
18.1	.000,004,0	"
18.5	.000,004,0	"
25.8	.000,004,0	"
28.0	.000,004,0	Beating
28.8	.000,004,0	Stopped
34.4	.000,004,0	"
37.2	.000,003,5	"
45.3	.000,003,5	Beating
49.0	.000,003,5	"
37.6	.000,003,0	"

GUINEA PIG METHOD.

F. E. DIGITALIS NO. 416233.

Weight of pig in Grammes	Dose per Gramme	Result
709	.000,5	Recovered
786	.000,5	"
825	.000,5	"
467	.000,5	Died
524	.000,5	"
694	.000,6	Recovered
701	.000,6	"
814	.000,6	Died
835	.000,6	"
744	.000,7	"
517	.000,7	"
481	.000,8	"

F. E. DIGITALIS NO. 335929.

750	.000,4	Recovered
340	.000,4	"
736	.000,4	"
680	.000,4	"
815	.000,5	"
630	.000,5	"
737	.000,6	"
772	.000,6	"
737	.000,7	Died
725	.000,7	"
531	.000,7	"
552	.000,7	Recovered
731	.000,8	"
538	.000,8	Died
375	.000,8	"

ONE-HOUR FROG HEART METHOD. VARIETY RANA PIPIENS. TEMP. 20° C.

F. E. DIGITALIS.

No. 416233.

Weight of frog in Grammes	Dose per Gramme	Result
40.9	.000,50	Beating
42.9	.000,60	"
39.1	.000,60	"
34.0	.000,70	"
46.5	.000,70	"
42.2	.000,75	"
50.8	.000,80	"
38.8	.000,80	"
31.2	.000,90	"
38.2	.000,90	Stopped
31.4	.001,00	"
35.5	.001,00	"

F. E. DIGITALIS.

No. 335929.

28.9	.000,90	Stopped
22.0	.000,80	"
21.0	.000,70	"
27.6	.000,70	"
23.0	.000,70	"
30.5	.000,70	"
42.9	.000,70	"
19.3	.000,65	Beating
20.2	.000,60	Stopped
23.5	.000,60	"
36.5	.000,60	"
37.4	.000,60	Beating
36.5	.000,50	"

The assays of these preparations by other methods have been inserted here, with the belief that they will be of some interest to the reader if closely analyzed, although no decided conclusions can be drawn from so small a number. Considering F. E. Digitalis No. 416233 and No. 335929 by the guinea pig and frog heart methods, it will be seen that while they show almost the same result on the guinea pig, there is a decided difference on the frog's heart. A lack of relationship in the results obtained by these two methods has been observed by others. Remembering that these fluids test the same on the guinea pig, consider the assays by the

cat method where No. 416233 is decidedly more active than No. 335929, the reverse of what was found by the frog heart method.

Attention should be called to the lot of animals used for No. 335929, which was perhaps the least suitable of any. It may be noticed that the greater number were females, varying considerably in size, some being in different stages of lactation. (No. 6 was in the early stage and had exceptionally large glands.) The males were all large and the results, perhaps a coincidence, varied somewhat in relation to the weight:

	Weight	Result
No. 2	3.18 Kgms.	.140,3
No. 8	3.00 Kgms.	.127,8
No. 10	2.46 Kgms.	.090,8

The assays on the two samples of strophanthus seed are almost identical by the frog heart method, and show but a small difference by the cat method.

Discussion.

Animals.—Hatcher and Brody selected cats in preference to dogs, and I believe rabbits, for several reasons, namely: "Accuracy afforded, facility with which they may be obtained, ease with which they may be handled, cheapness, and the fact that their use does not affect the sensibilities of the sentimental portion of the community to the same extent that the employment of the dog does." Having used no other animals for this particular method, I cannot remark on the point of accuracy. My experience has been that there is little in their favor regarding cost, all things considered. Cats are easily handled, though to my mind are no more so than dogs, or rabbits, except that in the case of the latter greater care is necessary in regard to any dissection or the giving of anæsthetics. I have found them far more difficult to obtain than rabbits and hardly less so than dogs. Whether their use affects the sensibilities of the sentimental portion of the community less than that of the dog seems questionable. At any rate, the use of cats certainly does affect the sensibilities of many people, and the procuring of a sufficient number of animals for this piece of work has been the source of considerable trouble. And for a manufacturing plant of this size, to secure enough cats to carry out the routine assays on the several members of the digitalis series, would be a practical impossibility. If some easily procurable animal such as the rabbit could be used for

this work, then one great difficulty would be removed. This point is of immense importance to the manufacturer by whom nearly all of the practical physiological assaying will always be done.

Having experienced difficulty in buying cats, an attempt was made at this laboratory to raise them, but this met with poor success. It has seemed that only under the very best conditions can cats be kept well for any considerable length of time. It has been our not infrequent experience that cats will refuse sweet milk and raw beef for some time after having been received, and while an abundance of food has been supplied, our cats have usually lost in weight.

When cats are needed for this work they should be made to fast for at least twenty-four hours, as otherwise vomiting will frequently occur, particularly under digitalis. Greater accuracy can also be obtained in regard to the weight.

Lactating animals cannot be depended upon as they seem to possess a greater tolerance for the drug, the degree depending on the stage of lactation.

The Period and Rate of Injection. The lethal dose of any of the digitalis bodies cannot, of course, be told at the outset. This is indeed the figure sought. Therefore, " 50 per cent. of the lethal dose " is a quantity which can only be widely approximated by one's experience with the given preparation. Whether this point in itself is a matter of great importance, within certain wide limits, I am unable to say. It would seem to be of importance, however, that the injection of all of these drugs be proportioned as evenly as possible over the ninety minutes. After one has injected an amount of digitalis, for example, and has waited the twenty minutes, he is ready to proceed with the ouabain solution. Since he does not know the value of the digitalis, he does not know, consequently, how much ouabain solution it will be necessary to inject during the following period of one hour. And not knowing this point, he is unable to judge how rapidly to inject. If he calculates on 5 c.c. when 10 c.c. would actually be required, then he will come to the end of the ninety-minute period with the animal still alive, and he must cautiously proceed with the probable result that one hundred and five minutes or so will be covered in completing the experiment. And having injected at a slower rate possibly a larger amount of ouabain may have been required. On the other hand, if he calculates on 10 c.c. when only 5 c.c. are necessary, he may kill the animal before the end of the period—perhaps in seventy-five minutes. And having

injected at a more rapid rate possibly less ouabain may have been used than would have been under normal conditions.

It might be remarked that the first experiment would furnish these points. This might be true, still, it might happen that the results from number one would be exceptional. Then the operator would be thrown off on number two, and when he found the results from number two quite different, number three would be necessary in order to tell which was more nearly correct.

If these points are of no importance then it would seem that the time limit of ninety minutes would be of no importance.

Number of Animals and Time.—In general it would seem that at least three experiments would be necessary in order to determine with confidence the strength of a preparation. If two out of three results checked quite closely, as under F. E. Digitalis No. 405467 (.113,5, .115,2), that number might be sufficient. Under strophanthus seed No. B-565, however, the results show a gradual increase up to the sixth experiment (.001,19, .001,37, .001,53, .001,66, .001,88), and under F. E. Digitalis No. 416233, results Nos. 1, 4, and 6 check each other rather closely (.077,3, .086,1, .087,4), and Nos. 2, 3, and 5 at a different figure check each other even more closely (.065,8, .068,2, .068,8).

If three or four experiments were sufficient, then an assay could be made in one day, a point in favor of the method. This would require one person's entire time and attention for the four and a half or six hours, besides part of the time of an assistant. At that, more actual time would be required than for any of the other methods.

Ease of Manipulation and Accuracy.—The method seems simple, and still, all points considered, it is the most difficult of all with which I am acquainted.

My results have been quite disappointing. They show variations for the different preparations, as follows:

Ouabain	123.3 per cent.
Excluding results Nos. 2, 4, 8, and 25	61.4 per cent.
Strophanthus Seed No. B-565	57.9 per cent.
Strophanthus Seed No. B-566	48.3 per cent.
F. E. Digitalis No. 405467	19.0 per cent.
F. E. Digitalis No. 416233	32.8 per cent.
F. E. Digitalis No. 335929 (excluding lactating animals)	90.5 per cent.
Excluding lactating animals and No. 1	53.0 per cent.
Tr. Digitalis No. 2-B (excluding Nos. 3 and 5)	67.8 per cent.

My results with crystalline ouabain would indicate that the lethal dose of this substance varies considerably with different animals. It seems, then, irrational to estimate the value of a preparation of digitalis, from its supposed equivalent of a body which is in itself, for any given animals, an unknown quantity. The authors of this method claim that crystalline ouabain will exactly replace digitalis in regard to its toxicity on the cat. It seems to me, however, that there might be some variance in its power to exactly replace different samples of digitalis depending on the proportion of active principles present and the conditions of these principles, whether or not decomposed. Since the amount of digitalis to be injected which will represent 50–75 per cent. of the required amount is an unknown quantity, it necessarily follows that the amount of ouabain required to complete the experiment, even if its toxicity could be exactly known, is an unknown quantity. Therefore, not knowing the amount of ouabain required, the rate of injection, which probably plays an important part, cannot be known. Lastly, the time required to kill, being dependent on the rate of injection, constitutes another unknown factor. So, when testing a sample of digitalis, one has to deal with six or more unknown factors. This requires an operator of considerable experience and skill.

Summary.

Considering the results of this work, together with my experience with the other methods, I am led to make the following statements in conclusion:

The cat method of Hatcher and Brody is unquestionably the most complicated and difficult of all the American methods, requiring an operator of considerable experience in animal experimentation.

It is *not* a method that will be found convenient and generally serviceable by the retail pharmacist.

It is more time-consuming than the other methods, requiring constant attention when started.

The item of expense, like that of the guinea-pig method, is decidedly in its disfavor.

The procuring of a sufficient number of suitable animals is a practical impossibility for the manufacturing pharmacist having a large number of preparations to test. This may also be the source of much unpleasantness and trouble.

Lactating animals cannot be depended upon as they seem to possess a greater tolerance for the drug, the degree depending on the stage of lactation.

While individual results will not infrequently check each other very closely, considering the results of an entire assay, great variations will often be observed, amounting in some cases to more than 100 per cent.

When testing a preparation one has to consider six or more unknown factors, namely:

1. Toxicity of ouabain.
2. Power of ouabain to exactly replace the digitalis bodies.
3. Amount of digitalis to be injected.
4. Amount of ouabain to be injected.
5. Rate of injection.
6. Time.

This method has perhaps one point of superiority over all others in that the matter of absorption is entirely eliminated.

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ABSTRACTS OF PAPERS READ AT THE BRITISH PHARMACEUTICAL CONFERENCE

By John K. Thum, Ph.G. Pharmacist at German Hospital, Philadelphia.

Portsmouth, the great naval port of the United Kingdom, was the scene of the forty-eighth anniversary of the foundation of the British Pharmaceutical Conference.

The sessions opened on Tuesday morning, July 25, 1911. Mr. William Frederick Wells, the President of the Conference, who is one of the best known pharmaceutical chemists of Ireland, and whose knowledge of the laws pertaining to pharmacy in the Emerald Isle is most comprehensive, devoted a considerable portion of his his presidential address to a discussion of the laws appertaining to pharmacy in the United Kingdom.

He commenced his address by speaking feelingly of the irreparable loss which British pharmacy sustained through the death of

John Attfield. Professor Attfield was President of the Conference for two years, in 1882 and 1883. He was one of the best minds in the scientific circles of pharmacy, a leader, with great ability, and untiring energy in the cause of pharmacy. "As a teacher he had great opportunities of bringing the best out of his pupils."

Mr. Wells then went on to speak of the craze for cheapness in the purchase of medicines by the public; medical records, he states, show that many valuable lives are sacrificed by this craze for low prices and the use of worthless drugs.

Specialization is the tendency of modern times, and he argues that if pharmacists want success in their calling they must specialize. The confidence of the public is only obtained by those who are best fitted to serve it efficiently. "The moment pharmacy is lowered to the level of a general business, as is being done so largely in our day by department stores and by limited companies of persons without any knowledge of pharmacy, whose sole object is to 'make money—honestly, if ye can, but make money'—then the fine art of professional dispensing is lost, and in many cases the public health suffers."

He then proceeded to deal with his chief theme, namely, the pharmacy laws of the United Kingdom. The Pharmacy and Poison laws, he states, were passed solely for the protection of the King's subjects and not for the benefit of the dispensing chemist. He then contrasts the laws with those of French and German Pharmacy. The essential difference in principle between their own pharmacy laws and those of France is that the French laws give the pharmacist a definite place in the community, certain services to perform for the community, and ensure that none shall poach upon the preserves fenced by these laws. No one may commence the study of pharmacy in France until satisfactory proof is given that the applicant's preliminary training is adequate. The requirement being a degree in Arts, Mr. Wells calls attention to the fact that the French law confers on pharmacists the sole right to dispense medical prescriptions, the only exceptions being in remote villages, where no pharmacists are in business, and only then are doctors allowed to dispense medicines. In discussing the German pharmacy laws the interesting fact was brought out that a custom exists there which is unknown in Great Britain, France or our own country, of strictly limiting the number of pharmacies, each pharmacy throughout the empire being licensed by the State. The result is that an apotheker cannot start business until a vacancy for a pharmacy occurs and he obtains

or purchases the concession to carry on the business of an old-established pharmacy or to open a new one where the growth of the population warrants, the State granting a new concession.

Mr. Wells also discussed several other acts or laws of Great Britain which are closely connected with pharmacy, the most important the Sale of Food and Drugs Act. He states that there is room for improvement in this act. It should be amended so as to make conviction certain when fraud is clear; too many technicalities are available under which offenders escape punishment.

Among the interesting communications brought to the attention of the Conference were the following papers:

Further Note on Podophyllum Emodi.

By John C. Unmey.

The writer mentions the difference of opinion regarding the therapeutic value of the resins of the two species of podophyllum—the American, *Podophyllum peltatum,* and the Indian, *Podophyllum Emodi.* He thinks this matter should be settled before the next British Pharmacopœia is issued.

The result of chemical and physiological tests brings him to the conclusion that a reasonable method of judging the resin is by means of podophyllotoxin assay. He gives such a method.

The Supposed Loss of Morphine in the Preparation of Tincture of Opium.

By E. H. Farr and R. Wright.

The authors state that from time to time statements have been made to the effect that in the conversion of opium into extract or tincture a loss of alkaloid results, or, rather, that the quantity of morphine shown by the official assay of a sample of opium is always greater than the amount found in the finished product, even when the utmost care has been taken to secure perfect exhaustion of the drug. The authors carried out some experiments with the view of testing the accuracy of these statements. They also give their method. They find that when official methods are followed throughout there is always a loss of morphine. They think that the loss is probably due to occlusion of the alkaloid, making its complete extraction by water or alcohol a matter of much difficulty.

Extract of Indian Hemp.

By Harold Deane.

The author says that as it is generally admitted that the resinous portion of the extract contains the active principle, and therefore extracts which are practically pure resin may be expected to be therapeutically more active. The author gives a simple and economical method for obtaining such an extract, which consists in washing away the brown extractive with warm water, after the alcohol has been distilled off.

Note on Spirit of Sal Volatile.

By E. W. Pollard.

For the preparation of sal volatile the writer recommends the following:

Oil of nutmeg	4½ drachms
Oil of lemon	6½ drachms
Water	2 pints

Distil one pint, mix with six pints of alcohol.

Dissolve ammonium carbonate 4 oz., in strong solution of ammonia 8 oz., water 9 oz., by the aid of gentle heat. Add this solution to the alcoholic solution of oils. In our opinion there is no necessity for even "gentle heat."

A Suggested Standard for Thyroideum Siccum.

By Reginald R. Bennett.

As it is agreed among most pharmacists that the activity of thyroid is dependent upon the combined iodine present the author of this paper thinks that an iodine standard should be made official. He gives a method for determining the iodine which is practically the same as Baumann. He also states that an iodine standard of 0.15 per cent. could be adopted for thyroideum siccum without in any way unduly harassing the manufacturer.

Linimentum Ammoniæ.

By F. H. Alcock.

The author briefly mentioned the various devices used to prevent solidification caking, and partial separation, of linimentum ammoniæ. As a result of experiments made by him he advises the following

method, which consists in reducing the amount of water in the preparation to a minimum, as giving effectual results:

Almond oil	3 ozs.
Olive oil	8 ozs.
Strong solution of ammonia (0.880 of commerce)	1 oz.

Note on Spirit of Nitrous Ether.

By D. B. Dott.

The author makes the proposition that no spirit of nitrous ether should be kept in stock at all because of liability to deterioration. As is well known this loss is occasioned by the volatilization of ethyl nitrite. He advises the use of two solutions, like Fehling No. 1 and No. 2 for the extemporaneous preparation of this spirit; the procedure being to mix a ½ dram of solution of sodium nitrite with 7½ drams of acidified alcohol to make 1 oz. of spirit of nitrous ether. He also suggests the use of lactic acid for acidifying the alcohol.

Note on Bartsia Odontites.

By H. Finnemore and G. E. Town.

Bartsia Odontites is a very common wayside plant of the natural order of *Scrophulariaceæ,* and although no toxicity has been ascribed to it, it is well known to be avoided by cattle. The authors bearing in mind the fact that plants botanically related often contain similar chemical constituents, it occurred to them that this relative of digitalis might possibly be worthy of pharmacological as well as chemical investigation.

Fourteen pounds of the whole plant were collected when in flower, dried in the sun, and completely extracted with hot alcohol in a continuous extraction apparatus. The resulting solution was concentrated and a sample tested on frogs. It was shown that it had no poisonous or digitalis-like effect. On allowing the alcohol solution to stand twenty-four hours a fairly large amount of crystalline matter separated in a nearly pure condition. The crystals proved to be mannitol. Identification was obtained by their composition, melting-point, and by their acetyl derivative.

Other papers read at Conference were: "The Moisture and Ash-content of Medicinal Extracts," by K. C. Allen and Theo. Brewis; "Note on Arsenates of Strychnine," by D. B. Dott; "Note on Strychnine Hypophosphite," by D. B. Dott; "Note on Solution of

Sodium Ethylate," by H. Finnemore; "An Experiment in Peppermint Culture," by H. John Henderson; "The Composition of Diabetic Foods," by F. W. F. Arnaud; "Note on the Constitution of Commercial Bismuth Subchloride," by J. Bristowe P. Harrison; "White Precipitate and the Analysis of White Precipitate Ointment," by G. D. Elsdon.

PRESIDENT TAFT'S ACTION UPON THE RECOMMENDATIONS OF THE COMMITTEE ON PERSONNEL OF THE U. S. DEPARTMENT OF AGRICULTURE.

President Taft's opinion of Doctor Harvey W. Wiley and his conduct of the Bureau of Chemistry (see this JOURNAL, pp. 381 and 388) has been in the hands of the public since September 16, 1911. The President's opinion, as embodied in his letter to the Secretary of the U. S. Department of Agriculture, carries no word of criticism, but many a word of praise.

Speaking of the Congressional investigation into the Department of Agriculture, Mr. Taft says:

"The broader issues raised by the investigation which have a much weightier relation than this one to the general efficiency of the department may require much more radical action than the question I have considered and decided.

"The nub of the charge by the personnel board was that Doctor Wiley, Doctor Kebler, Doctor Bigelow and Doctor Rusby in effect conspired to put on the record a contract for a general employment of Doctor Rusby's services for $1,600 a year, but actually and secretly made a contract with him by which he was only to do enough work during the year for the $1600 to secure him a compensation of $20 a day and that this was done in deliberate and defiant violation of the law was interpreted by the Attorney-General in the opinion already referred to, in which he held that Congress had limited the compensation of experts to $9 a day.

"After you submitted to me the report of the personnel board I asked the Attorney General to examine it and give me his opinion in respect to the matter. He did so and advised me that the recommendations of the personnel board ought to be carried out. In connection with his recommendations, he invited attention to a clause in the appropriation bill of March, 1907, still in force, that enjoins upon the head of each department the duty of exacting from the

employes in that department who are under an annual salary labor amounting to seven hours a day.

"An examination of the records satisfied me that the questions had not been presented to the persons involved in such a way as to enable them to make full defense. They had only been called as witnesses, and cross-examined without a full understanding that they were under trial which might involve their dismissal. Accordingly I directed you to submit the whole record to each one of the persons charged and invite from him an answer.

"The answer of Doctor Wiley specifically denies that he ever saw the correspondence between Doctor Kebler and Doctor Rusby or that he ever consciously entered into an agreement by which Doctor Rusby was in effect to receive compensation at a rate in excess of that prescribed by the statute as interpreted by the Attorney-General.

"The truth is, it appears from the answers of Doctor Wiley, Doctor Kebler and Doctor Bigelow that there had been a good many precedents in the department which seemed to justify the employment of Doctor Rusby at an annual salary when it was not expected that his entire time would be taken up. This was the case with respect to the employment of what was known as the Remsen Board.

"Solicitor McCabe, to whom I referred the question of precedents made in the case, replied that in the practice of the department the clause in the appropriation act of March 5, 1898, had been held to have no application to the employment of experts outside of Washington.

"It is necessary fully to understand this difference between the attitude of the department toward an employment at an annual salary of this kind, and the opinion of the Attorney-General in this matter, because if Doctor Wiley and his associates had understood that the $1600 annual salary required them to exact from Doctor Rusby seven hours a day for all the work days of the year, then, of course, his employment must have been known by them to be illegal and under the circumstances, to be only a cover for a different contract of employment; but if they understood, as seems to have been the case generally in the department, that such an employment at an annual salary might be entered into with experts of this kind, and only subject the experts to an obligation to work for the department whenever called upon, with the understanding that they had

some other vocation to which their chief attention was given, it clearly reconciled the action of Doctor Wiley with a desire to comply with the law.

"The recommendation of the Attorney-General given to me was upon only part of the evidence, and hence his judgment was different, doubtless, from what it would have been if he had had the whole record before him, as I have now.

"It seems fairly clear that Doctor Wiley, after an examination of the records, concluded that the employment of Doctor Rusby at \$9 a day for laboratory work and \$50 a day for court work would amount to \$1600 a year if the department called on him whenever they needed him, and that it was this arrangement to which you consented. In Doctor Kebler's anxiety to induce Doctor Rusby to accept the new terms of employment he certainly betrayed a willingness to construe the contract of employment of Doctor Rusby at \$1600 a year in one way to reconcile it with the law and in another way to satisfy Doctor Rusby in his wish to secure \$20 a day, and I think he ought to be reprimanded for his disingenuous conduct in writing such letters as he did. He said that he did not intend to violate the statute as interpreted by the Attorney-General, and, indeed, that he did not know exactly what the ruling was; but whether he did or not, the language of his letters does not have a commendable tone and suggests a willingness to resort to evasion that calls for official reproof.

"Here is the pure food act which is of the highest importance to enforce, and in respect to which the interests opposed to its enforcement are likely to have all the money at their command needed to secure the most effective expert evidence. The Government ought not to be at a disadvantage in this regard and one cannot withhold one's sympathy with an earnest effort by Doctor Wiley to pay proper compensation and secure expert assistance in the enforcement of so important a statute, certainly in the beginning when the questions arising under it are of capital importance to the public.

"If this were a knowing, wilful, deliberate effort to evade the statute as construed by the Attorney-General, accompanied by a scheme to conceal the evasion and violation, I should think the punishment recommended by the personnel board and concurred in by the Attorney-General was none too great; but an examination of the whole case satisfies me that a different construction ought to

be put upon what was done; that the evidence does not show that Doctor Wiley was a party to the correspondence or the letters upon which the chief charge is sounded, and that his action in the matter was only in accord with previous precedents in the department which justified him in doing what he did.

"With respect to the other persons charged, I find an over zeal in Doctor Kebler and Doctor Bigelow, which prompted a disingenuous method of squaring Doctor Rusby's desire for what he thought was adequate compensation with the contract which you and Doctor Wiley were willing to make with him and that for this Doctor Kebler and Doctor Bigelow should be reprimanded by you. So far as Doctor Rusby is concerned with respect to this particular contract I do not find him at fault. For purposes of punishment or dismissal, I cannot charge him with knowledge of the legal difficulties involved in his employment. I examined the record in this case a number of weeks ago and I reached the conclusion which I have stated here, but meantime, a committee of the House of Representatives deemed it proper to institute an investigation into the Department of Agriculture, and especially into the Bureau of Chemistry and its relation to the department generally.

"It seemed to me, under these conditions that perhaps it was wiser for me to delay until the investigation was completed and the report of the committee made. The committee has not made a report, although I believe the evidence has been substantially closed and will not do so until the next session of Congress.

"Further consideration satisfies me that there are much broader questions involved in the investigation and the evidence there brought out than in the present charge, which is narrow and definite and can now be properly disposed of. The broader issues raised by the investigation which have a much weightier relation than this one to the general efficiency of the department may require much more radical action than the question I have here considered and decided.

"There is another charge against Doctor Rusby for securing the appointment, on the common laborers' rolls, of a physician and expert whom he could use to do his work at a small stipend, when he himself was called away in other employment. I regret to say that the arrangement which Doctor Rusby thus made is not especially creditable to him and shakes in some degree one's confidence in his avowed wish to make personal pecuniary sacrifice in the public inter-

est for the enforcement of the pure food law. But Doctor Rusby's position as an expert of high standing is such that I do not think that any more than this expression of opinion should be imposed as penalty. My information is that the Government needs his services, that he has already rendered valuable aid and that the error referred to committed by him should not call for any further action or remark.

"You will communicate the result to the personnel board, and also to the persons charged. Sincerely yours,

"WILLIAM H. TAFT."

THE NEW ADMISSIONS AND DELETIONS TO THE U. S. PHARMACOPŒIA IX.

At the Boston meeting of the American Pharmaceutical Association, Prof. Joseph P. Remington, Chairman of the Revision Committee of the U. S. Pharmacopœia, submitted the names of the articles proposed for admission and deletion to the 9th revision of the U. S. Pharmacopœia. As most of the substances are retained, the names of only those articles which are "dropped" from the Pharmacopœia and those have been proposed for admission are printed at this time.

LIST OF ARTICLES DROPPED FROM THE PHARMACOPŒIA.

Acetum Opii
Acidum Camphoricum
Acidum Sulphurosum
Alumini Sulphas
Argenti Nitras Mitigatus
Bismuthi Citras
Bismuthi et Ammonii Citras
Calamus
Cassia Fistula
Cataplasma Kaolini
Ceratum Camphoræ
Ceratum Plumbi Subacetatis
Cerii Oxalas
Chimaphila
Chirata
Cinnaldehydum
Colchici Cormus
Collodium Stypticum
Confectio Sennæ
Conium
Cusso
Cypripedium
Emplastrum Hydrargyri
Emplastrum Opii
Emplastrum Saponis
Emulsum Chloroformi
Emulsum Olei Morrhuæ cuf Hypophosphitibus
Extractum Colchici Cormi
Extractum Digitalis
Extractum Hæmatoxyli
Extractum Krameriæ
Extractum Leptandræ
Extractum Malti
Extractum Scopolæ
Extractum Sumbul

Ferri Citras
Ferri et Ammonii Sulphas
Ferri et Ammonii Tartras
Ferri et Potassii Tartras
Ferri et Strychninæ Citras
Ferri Hydroxidum
Ferri Hypophosphis
Ficus
Fluidextractum Calami
Fluidextractum Calumbæ
Fluidextractum Chimaphilæ
Fluidextractum Chiratæ
Fluidextractum Conii
Fluidextractum Cubebæ
Fluidextractum Cypripedii
Fluidextractum Digitalis
Fluidextractum Euonymi
Fluidextractum Eupatorii
Fluidextractum Geranii
Fluidextractum Lappæ
Fluidextractum Leptandræ
Fluidextractum Lupulini
Fluidextractum Matico
Fluidextractum Mezerei
Fluidextractum Pareiræ
Fluidextractum Phytolaccæ
Fluidextractum Quassiæ
Fluidextractum Quercus
Fluidextractum Quillajæ
Fluidextractum Rosæ
Fluidextractum Rubi
Fluidextractum Sabinæ
Fluidextractum Sanguinariæ
Fluidextractum Scopolæ
Fluidextractum Scutellaria
Fluidextractum Stillingiæ
Fluidextractum Stramonii
Fluidextractum Veratri
Geranium
Glyceritum Ferri, Quininæ et Strychninæ Phosphatum
Hamamelidis Cortex
Hedeoma
Hyoscyaminæ Sulphas
Infusum Pruni Virginianæ
Iodolum
Lappa
Lithii Benzoas
Lithii Salicylas
Mangani Sulphas
Mastiche
Matico
Mistura Ferri Composita
Mistura Rhei et Sodæ
Mucilago Ulmi
Naphthalenum
Oleatum Quininæ
Oleoresina Lupulini
Oleum Adipis
Oleum Aethereum
Oleum Chenopodii
Oleum Copaibæ
Oleum Erigonerontis
Oleum Sabinæ
Pilulæ Aloes et Mastiches
Pilulæ Aloes et Myrrhæ
Pilulæ Laxativæ Compositæ
Pilulæ Opii
Pilulæ Podophylli, Belladonnæ et Capsici
Prunum
Plumbi Iodidum
Plumbi Nitras
Potassii Sulphas
Prunum
Pulvis Morphinæ Compositus
Quercus
Quillaja
Rubus
Sabina
Santonica
Scammonium
Scoparius
Scutellaria
Sodii Bisulphis
Sodii Nitras
Sodii Pyrophosphas
Spiritus Aetheris Compositus
Sulphuris Iodidum
Syrupus Ferri, Quininæ et Strychninæ Phosphatum
Syrupus Hypophospitum Compositus
Syrupus Krameriæ
Syrupus Rubi
Tamarindus
Tinctura Aloes et Myrrhæ

Tinctura Cardamomi
Tinctura Gallæ
Tinctura Ipecacuanhæ et Opii
Tincturæ Herbarum Recentium
Trochisci Gambir
Trochisci Glycyrrhizæ et Opii
Trochisci Krameriæ
Trochisci Santonini
Unguentum Gallæ
Unguentum Hydrargyri Oxidi Rubri
Unguentum Potassii Iodidi
Unguentum Veratrinæ
Unguentum Zinci Stearatis
Viburnum Opulus
Vinum Album
Vinum Cocæ
Vinum Colchici Seminis
Vinum Ergotæ
Vinum Ferri
Vinum Ferri Amarum
Vinum Ipecacuanhæ
Vinum Opii
Vinum Rubrum
Zea
Zinci Bromidum
Zinci Iodidum

NEW ARTICLES PROPOSED FOR ADMISSION TO THE U. S. PHARMACOPŒIA IX.

Ammonium Bifluoride
Antitetanic Serum
Apiol
Aspidospermine
Bismuth Beta-Naphthol
Buchu (Long)
Caffeine Sodio-Benzoate
Calcium Chloride (Hydrated Crystals)
Calcium Glycerophosphate
Calcium Lactate
Carbonic Acid (Compressed)
Condurango
Creosote Carbonate
Crocus
Diacetyl-Morphine
Diacetyl-Morphine Hydrochloride
Diastase
Emplastrum Cantharidis
Erythrol Tetranitrate
Fluorescein
Hydrastine Hydrochloride
Mercury Salicylate
Milk of Magnesia
Milk of Bismuth
Oxygen (Compressed)
Picric Acid
Phenolphthalein
Pine Needle Oil
Potassa Sulphurata
Quinine and Urea Hydrochloride
Saccharin Sodium Salt
Sodium Cacodylate
Sodium Glycerophosphate
Sodium Perborate
Solution of Hydrogen Dioxide (30 per cent.)
Theobromine Sodio-Salicylate
Trioxymethylene.
Uranium Nitrate
Vaccine Virus

There are thirty-eight articles still under consideration for admission.

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INSECTS DESTRUCTIVE TO BOOKS.[1]

(SECOND CONTRIBUTION.[2])

By William R. Reinick.

" The man who marks a borrowed book,
And makes the ends and corners look
Dog-eared and ragged and infirm,
He is an insect and a worm."

Ella Wheeler Wilcox.[3]

It will be impossible in this lecture to go into details regarding the various series of experiments that have been made and studied in order to obtain the results, which I will speak of this evening, on account of the limit of time. Some of my remarks will appear to some researchers to be the words of one lacking an understanding of the groundwork of science, but in reply to those who doubt, I can only say, investigate along the same lines and the results will amply repay you for your time and labor.

Paste-eaters.—The statement previously made by me to the effect that the paste used in binding was often eaten by the larvæ of insects hatched from eggs that were originally in the flour, has been questioned on the ground that the heat necessary to boil paste, 212°, would have killed all life. How this challenge could have been made by anyone who had experimented on the vitality of eggs under adverse conditions is beyond my comprehension. They confuse the life that has hatched with the life within the egg. Heat no doubt would destroy the greater portion of the life that had hatched, but

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[1] Copyrighted by the author, 1911.

[2] A lecture delivered at the University of Pennsylvania, 1911.

[3] From a manuscript in the author's collection.

not always, as in the case of certain bacteria, who from their known power to withstand a high degree of heat, are popularly called heat-lovers. They have even stood the high temperature of steam for a number of hours. But aside from the imago state of the insect, the egg, in which the embryo passes through its various stages, has been overlooked, and experiments properly conducted will prove them capable of withstanding a temperature very much above that which the scientist of to-day has knowledge.

Anyone caring to investigate the life in the paste may easily do so in the following way: Boil the flour in the usual manner, adding the glue for the binder, and after allowing the mass to cool, let it stand in a dark, damp place. After it has become sour, it will be found that nature will again produce the same forms from it as she did when it was in the form of flour. Naturally, to give conclusive evidence, care must be taken to see that no insects are allowed to gain access to the paste from the outside, so as to avoid any possibility of their laying their eggs in the substance.

Bindings: Wood Bindings.—Books that are bound with wood covers are always subject to the borings of the insects that lived on the species of trees from which the boards are made, especially if the atmosphere is saturated with moisture, this being due to the porous nature of the wood. Take the point of a needle, touch the wood, and you find that it gives, showing that it is composed of cells containing gases. They are not only subject to attacks from without, but also from within; *i.e.,* larvæ hatching from eggs that were deposited in the tree before it was made into lumber. The early stages of a number of species of wood-destroying insects take quite a long period to evolve.

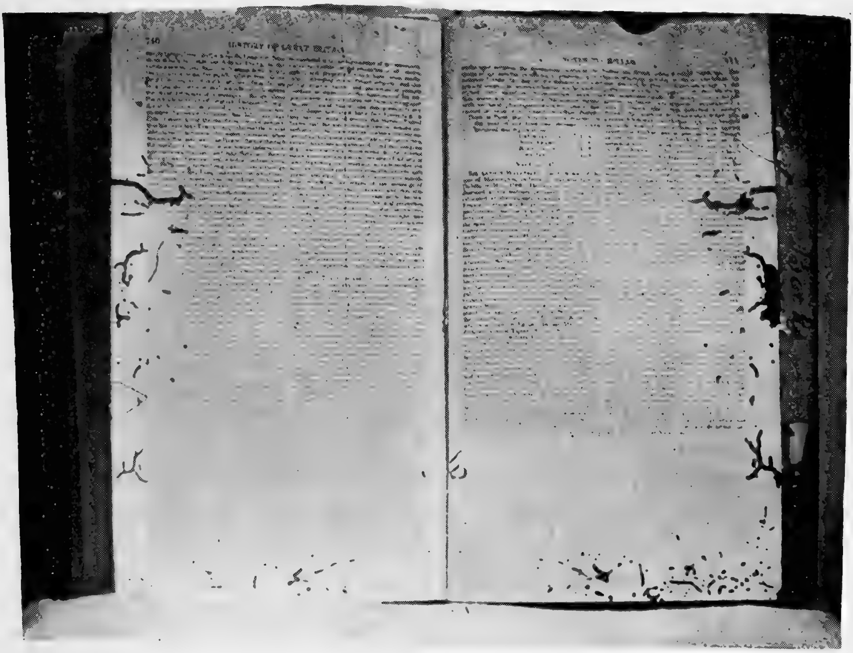
The insects destroying wood bindings are species of *Bostrychidæ* and some of the *Scolytidæ.* One species of *Cerambycidæ* has been named as causing trouble, and as a large proportion of the species of this family are wood-borers, other species will likely be found to tunnel these covers.

Bindings: Leather Bindings.—The so-called dry rot of leather bindings said to be caused by the fumes in the air, especially where gas is used for lighting purposes, is also found to take place with leather-bound books that have not been exposed to such chemicals. Investigation will prove that instead of gases being the destructive agency, minute forms of life alone are the cause.

Another subject for future research is the cause of certain round

holes, as though made by shot, often found in books bound in sheepskin. A careful examination of bindings showing these peculiar shot-like holes failed to show any galleries leading into or along the back of the books, which the *Coleoptera,* the insects named as committing these ravages, would make; and careful observation will reveal that instead of the holes being made by beetles, that a species of *Trichina,* a parasite which at present causes great losses to sheep-breeders, is the source. The skins, even after going through the

Fig. 1



Book from British Guiana. The volume is bored through by a species of *Coleoptera.*

various processes of tanning, still contain the same basic principles as in the primo state.

Bindings: Printed Cloth Bindings.—These bindings, on account of the oils and greases used in their manufacture, are subject to the ravages of those insects which have use for such substances.

Species of *Blattidæ* and *Gryllidæ* are fond of these bindings.

Printing Inks.—While investigating the various printing inks, Mr. Thomas A. Bradley, President of the Security Bank Note

Company, of Philadelphia, called my attention to the fact, that the working clothes of the employees of his company, if left hanging in a dark place for a time, were found to have been gnawed by the larva of some species of insect, and that the most striking part was, only that part of the clothing which had been stained with ink was eaten. Most inks contain one or more acids in their composition, and as they are claimed to be poisonous and therefore should kill, one would say that the parts of the goods discolored by the inks should be exempt from these attacks, instead of proving attractive. A French author writes of a book in which the insects had eaten the portion of the paper which had received the impress of the ink, showing that they were after something besides the paper, paste or binding.

To prove this, I took a piece of parchment—sheepskin and imitation—and a quantity of the finest grade of engraver's black printing ink, made a circle of ink in the centre with diagonal lines running from this to the corners and sides and a one-eighth inch border all around the edges. After the ink was dry, I placed a piece of each kind of parchment in a tin can with twelve roaches, adding water from time to time for drinking purposes. At the end of two weeks an examination of the parchment showed that the roaches had eaten all of the edges, had then followed the diagonal lines, eating mostly the portions so marked, and then the circle, showing that they knew the value to them of the acetic acid which was in the ink.

I hope that other experiments will be made along the same lines to ascertain if the various dyes, though often of the same color, are more secure from the inroads of insects than others, on account of containing certain chemicals in their composition. *Blatta orientalis* was the species used in making these experiments.

CONDITIONS FAVORABLE FOR THE PROPAGATION OF BOOK PESTS.

Darkness.—The majority of libraries generally keep a large number of their books upon stacks placed in a dark portion of the building, badly ventilated, and the only light available as a rule is from gas jets or incandescent lamps, which are only lighted when needed. This darkness (the necessary condition for the starting of all life), the more or less damp air which is found in these surroundings, the gases of various kinds in the air, and the fact that the books most seldom called for are kept in these locations, all combine to give

favorable conditions for the propagation of these small forms of life without much chance of their being disturbed during the evolution of their life-cycle.

Gases.—It is known that quite an amount of poisonous gas is given off by the gas used for lighting purposes, and also from the breath of readers, and that if the room is not properly ventilated, a quantity is constantly floating in the air. As plant life is known to live upon this gas, so will the lower forms of life be found to exist to a greater or less degree upon them.

In the earlier stages of the earth's history, when the chaotic conditions were in full play and harmony, every form of life was crude and drawn to the grosser matter that surrounded it for its energies and principles of growth. From the sun emanates the rays that have acted on the earth's surface and its interior, generating various elements known to science to-day to the extent of some seventy elements. By the action of these heat rays in associating the waters of the earth with these elements were generated gases, and these gases are the energies upon which the lower organic life live.

Man's body is a laboratory of life. While man uses intelligence in regards to poisons, the instinctive power of the little insect is used with greater care. Doctors will prescribe poisons and the patients take them without question, but the little insect uses its instinct to know what not to touch, and of those that it does partake, knows just how much to eat.

UNFAVORABLE CONDITIONS FOR THE INCREASE OF THESE INSECTS.

Light.—This, with cleanliness, are the two most important factors in preventing the ravages of insects among books, and will also prevent another sort of damage to books, which is the various kinds of fungi which start to grow upon and in the books a short time after they have been placed in a damp, warm atmosphere.

The lessening of the destruction of books by insects, that have been kept on shelves in badly-ventilated and badly-lighted libraries, after having been transferred to a new building having good ventilation and light, is ably illustrated by the experience of Mr. Ernest J. Reed, Librarian of the Oahu College, Honolulu, Territory of Hawaii. He stated in a letter to me that before the books were moved to the new building, the whole collection was constantly being riddled by various species of boring insects, but that since

moving to the new quarters they are comparatively little troubled by pests. From an examination of samples of books I have received from him, I wonder how anyone was able to read the books with any degree of satisfaction, as many had hundreds of tunnels running through them, some had large cavities eaten in them, and others looked as though a mischievous boy had taken a pair of scissors and tried to see how many strips he could cut each leaf into; in others the cloth binding was almost entirely eaten off, exposing the galleries made by the beetles in the cardboard covers. (Illustrations Nos. 1 and 2.)

Books will also be found to have forms of life living upon them which at present cause much speculation as to what substance they feed upon, and the insects commonly known as book-lice, belonging

Fig. 2

Volume from the Hawiian Islands. The cloth cover is almost entirely eaten, exposing in the strawboard the tunnels of *Catorama Mexicana*, a species of *Colecptera.*

to the family *Psocides* of the order *Corrodentia,* are examples. In turning over the pages of books or looking over papers which have been kept in a dark location for a long while, one with a keen eyesight will often see little specks of life run to a crevice to hide or get away from the rays of light. On account of their whitish gray color and an ability to run with a speed which is amazing when the

size of the insect is considered, it is only the keen observer who will spy them as they scamper across the printed page. Though so small, they will be found to be the cause of a great deal of damage to books.

Many investigators think that the greatest damage is committed by the larger forms, whereas, as a rule, the smaller species, in proportion to their size, consume many times the amount of food as compared to that of the larger insect. I especially noticed this in making the experiment on artificial parchment herein mentioned, where twelve roaches, many of them females, big with eggs, at which time, of course, in order to provide the necessary supply of food for the coming generation, they would eat more than before the period of gestation, ate such a small amount of the paper that I spoke about it to a gentleman who was present when I examined the parchment. A fly in one day will consume food equal to its own weight. This is also illustrated by birds, who, in proportion to man, eat a far greater quantity of food.

Researches.—During the past year, I have made a number of experiments, and much against my will have arrived at the conclusion that as far as our present knowledge of the effects of poisons on these small forms of life is concerned, we have not even laid the foundation upon which to build.

The potato bug is an example. The paris green is placed on the plant in the morning, but at night the bugs are still there and seem to be eating the plant with more voracity than when it was absent. The chemical elements in the air and plant cause a reaction to take place, by which the poisonous qualities are lost, and instead of poison to kill, a substance to the liking of the insect is produced, as I discovered during my experience in farming.

Another source of error is the lack of positive knowledge as to the resistance of these minute forms to poisons, heat, pressure, etc., in their early stages. I have been taken to task for the statement made by me in my first paper as to mosquitoes hatching from eggs that have lain exposed for a long period of time, but I think that the following example of life remaining dormant under adverse conditions is more wonderful.

When I started to collect insects, I used for a cabinet a case of drawers which had been kept in a dry room of my home and had been in daily use for about twelve years, and placed it in an outside shed, the atmosphere of which was warm and damp. Some time

after, upon looking at the contents of one of the drawers, I discovered a specimen of a large species of *Cerambycidæ* lying on the bottom and wondered where it came from. After searching on the outside and finding no opening, I pulled the drawer entirely out and discovered that the insect had emerged from the board used in making the side of the drawer, showing that while the case remained in a dry location, the life remained dormant, going on with its life cycle when the proper conditions were given.

Seeds stored in a dry location for quite long periods have been known to produce plants when placed in the soil, and anyone familiar with bacteriology knows the great vitality of these forms, invisible to the naked eye. The smaller forms also have bodies more capable of withstanding supposed remedies than the larger insects. Take one hundred roaches and the same number of red ants, pour boiling water on them, count the number of survivors of each kind, and you will find that all or mostly all of the roaches will have been killed, while a large proportion of the ants are still alive; an interesting line of experimentation for economic entomologists.

Remedies.—I have received letters from almost every country of the world suggesting remedies, some claiming success, but the majority acknowledging defeat; in many cases what was proclaimed to be a specific remedy by one writer was declared to be a failure by others.

Even books, treated with the strongest poisons, failed to give the desired results, but on the contrary the remedies seemed to give the insects that they were supposed to kill a new lease of life. In the case of experiments conducted by the United States Bureau of Standards,[4] and also by myself, the roaches (the insects experimented with) produced their young as though nothing unusual was taking place. The roach, although said to have a wonderful instinct, really has less than the smaller forms of insect life. A famous remedy for destroying roaches is made of a combination of sulphur and sugar, the sulphur causing a luminosity when the bait is placed in the dark. The roach is attracted by the glow that deadens its instinct which would otherwise warn it against the poison, and it eats the bait; but the little ant's instinct, not being

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[4] Memoranda relative to binding of publications for distribution to state and territorial libraries and designated depositories.—United States Congress, Washington, 1908.

affected by the light given off by the sulphur, warns it of the danger, and as a consequence it seldom eats a poison that is placed near its haunts. This Bureau made a very large series of experiments in order to obtain, if possible, a binding material which would be exempt from the inroads of insects, and also to withstand the effects of light and gases without fading, and which Prof. S. W. Stratton, the Director of the Bureau, very kindly loaned me for study. The tests were made with cloths, ducks and buckrams of various colors. A portion of each piece was chemically analyzed in order to find what substances were used in their manufacture, and the rest of each sample was exposed to the roaches for various numbers of days. The results, when tabulated, proved that it did not seem to make any difference as to what materials were used in the coating, many of which were poisonous, as they had nibbled all but one of the bindings. They then tried impregnating some of the samples with a weak solution of quinine and others with strychnine, but these failed to give the desired immunity; and, upon increasing the quantity of the poison in the solution, the attractiveness of the substances was increased. Even corrosive sublimate was ineffective. It is true that the insects died within a few days, but not until they had ruined the bindings. One sample, seeming to be exempt from their ravages, was selected and adopted by the Bureau as a standard for binding the United States Congressional documents, and also accepted by the American Library Association Committee on Book-Binding as the best binding for library books.

During a conversation in the Government Printing Office last winter, while being shown the various materials used for binding Government documents, I expressed doubts as to the buckram approved, known as No. 666, being insect-proof; and this opinion has since been confirmed by experiments made by the Philippine Bureau of Science, Dr. Stratton and myself.

My own experiments with a poison of an entirely different character gave better results. One-half of each of the various kinds of binding materials tested was treated with my preparation and the other half left untouched. They were placed in boxes and exposed to the attacks of the roaches for various periods. Upon examination, I found that while the coloring matter in certain samples had been eaten on both the treated and untreated portions, the poisoned portions of quite a number of the others were left alone. In some cases pieces of the same color, although of different

manufacture as regards to one sample, were eaten and the other piece was left undisturbed. The remedy used by me did not, to my knowledge, kill any of the insects. From a comparison of the results, I arrived at the conclusion that the material used for coating the buckrams, etc., in a number of cases, had neutralized the effective action of the preparation used by me, and that in order to really obtain a material that would be insect-proof, it would be necessary to use such coloring matters as would not overcome the beneficial action of the poisons.

The fact that insects seem to show preference for certain colors used in binding materials, has already been noticed by a few of my correspondents; and also by myself while making researches in Florida last summer.

The Philippine Bureau of Science, finding that the buckram used as a standard was not insect-proof in the Islands, made another series of experiments, and have produced material which they claim is absolutely safe, but as I have not received any samples to test, although I have made request for same, I am unable to pass judgment upon it.

Although scientists have been experimenting upon binding materials in order to obtain one that would be exempt from the ravages of these little insects, little has been done towards preserving the most important part, and which, according to my investigations, receives the greatest injury, namely, the printed portion of the book. Some experiments made by J. Rodway, Esq., Secretary of the Royal Agricultural and Commercial Society of British Guiana, with papers impregnated with sulphate of copper, turpentine, kerosene and corrosive sublimate, failed to stop the borings of the insects. I have sent boards and books made of different papers which I have treated with a substance to Mr. Rodway, and to other parts of the world, and the results as to the effectiveness of the remedy used should be received during the coming winter.

Arsenic in its various forms is used in large quantities in the materials used in book-making, though denied by the manufacturers; but chemical analysis will generally show the presence of this substance, which is of use to the insects. The elimination of arsenic in materials used in book-making would not only do away with a source of attraction to the insects, but save people from being poisoned, as anyone familiar with the literature of poisons knows.

Books as Disease Carriers.—Again, I speak upon the transmission of diseases by books, because the greatest disease carrier among insects that we know of to-day is the common house-fly, *Musca domestica,* which is also one of the book-destroying insects. There are a number of instances where the maggots of the fly have been found living upon paper, kept in damp places, but the damage done directly to the book is as nothing when compared to the damage done by their transferring germs, and, unless means are taken for their extermination, they will rank first among book enemies, because those who know of the fly's ability to carry disease germs, will refuse to read any book which the fly has stained. The common house-fly is only found around the habitation of man, showing that it has evolved from some other form which formerly lived in the open until it has now become thoroughly domesticated, as other forms have done, are doing, and will do in the future.

According to Dr. Howard, a single female fly in the spring might, therefore, become the progenitor of 195,312,500,000,000 flies by the end of the summer or mid-autumn, and allowing one million flies to a bushel makes over 193 million bushels, each one of whom is capable of spreading contagion. An investigation made at the Agricultural Experiment Station at Storrs, Connecticut, in 1908, upon 414 flies, showed that the number of bacteria on a single fly may range all the way from 550 to 6,600,000, an average of one and one-fourth millions bacteria on each, an almost incredible number to be found on such a small object. The objectionable class, coli-aërogenes type, was two and one-half times as abundant as the favorable acid type. Now this only includes those on the outside, and every bacteriologist knows that large numbers are found in the intestines and expelled with the excreta. Mr. N. A. Cobb, in his article "The House-Fly,"[5] states that a well-fed fly defecates 104 times in less than two hours, and that spores were found in fifty-five of the specks. These specks, containing germs, are laid upon the covers or pages of the books, and as personal observation shows that a very large portion of readers moisten their fingers in turning over the leaves of a book, it is readily seen how the fly speck upon the paper is moistened, adheres to the finger and the germs transplanted to the mouth, where they at once find the proper conditions and proceed to breed, resulting in the reader becoming afflicted with

[5] *National Geographic Magazine,* vol. xxi, 1910, pp. 371–380.

the disease, the source of which it is impossible to trace, on account of the slight consideration given by the medical world at the present time to books as a source of disease.

The danger of contracting disease by the fingers dampened with saliva in order to turn over the pages of a book is especially so in the case of persons suffering from tuberculosis, whose sputum contains millions of the bacilli. The saliva drying, the *Tubercle bacillus* cling to the fibre of the paper, and soon as another person, who also has the vulgar habit of wetting the fingers in turning the pages, uses the book, the germs are removed to fertile soil. Many other diseases, especially skin diseases, are without doubt frequently transmitted by this means.

In conclusion, I cannot speak strongly enough on the importance of cleanliness in preventing the destruction of books by insects, and the spreading of disease. The volumes in the library should be kept thoroughly cleaned, the attendants ought to clean their hands frequently, and the patrons compelled to wash their hands before using the publications and should not be allowed to wet the fingers in turning the pages. These precautions will help to decrease the spread of tuberculosis and other diseases, and do away with the grease stains on the paper, which are breeding grounds for germs and attractive feeding places for insects. Screens should be placed on all windows and doors to prevent the entrance of flies, and by these means only will the destruction of the stores of accumulated knowledge be decreased and a source of death be overcome.

Theory Confirmed.—As this article goes to press, I have just obtained results from an experiment which goes to prove that books may be damaged by the hatching of life from eggs which were originally in the flour, or most likely, the grain.

In June, 1910, I obtained from Mr. James Stone, of Philadelphia, three samples of flour which he claimed were absolutely pure and each of the three varieties were placed in a sealed Mason jar and the jars put upon a shelf in a closet. They were thus kept in a dark location and also a dry atmosphere. At various times these jars were examined, but no sign of life appeared until the examination made October 6, 1911, at which time I was very astonished to find that two of the samples, "spring wheat flour" and "rye flour," were literally covered with what appears by looking through the glass of the jars to be a species of *Psocidæ* or book-lice. The third

sample, "winter wheat straight," does not show any signs of life at the present time.

The results are quite startling, as it shows that the stages of some of these small forms take a period of time to evolve beyond our present knowledge, also that they did not need any oxygen to sustain them as the jars have never been opened since the flour has been placed in them, showing that the assertion made above, that many small forms live to a more or less extent upon gases supposed to be poisonous, had a foundation of truth. Lastly, that instead of one of the species known as grain-eaters appearing, that a species of *Psocidæ,* the habits of which are very little known, but I do not recollect that they have ever been classed as flour-eaters before, should appear in such immense numbers.

NOTE.—This article concludes the general outline of the divisions used by me, and I shall later publish a detailed account of each, giving descriptions and illustrations of the insects and examples of their work.

THE ASSAY OF JALAP.

By Horace North

Analyst with Lehn & Fink, New York.

Resin of jalap is defined as that portion of the drug soluble in alcohol and insoluble in water. The assay of jalap for resin is properly based on this definition.

Put 10 gms. of finely powdered jalap in a shallow porcelain basin having a diameter of about 16 cm., moisten the drug with 3 c.c. of water, granulate uniformly with the aid of a small glass pestle, transfer to a sheet of paper and thence into a 300 c.c. Erlenmeyer flask. Add 51 c.c. of 95 per cent. alcohol, connect the flask with a reflux condenser and heat in a water-bath so that the alcohol boils gently for about one hour. Lay a pledget of absorbent cotton in the bottom of a slightly conical percolator, saturate with alcohol, and press a perforated porcelain plate firmly down upon the cotton until the excess of alcohol has drained. Place the dish in which the drug was granulated on a water-bath, kept warm over a low flame, and support the percolator above the dish. Remove the flask from the water-bath, cover with a porcelain

lid and allow to cool somewhat. Pour the mixture of drug and extract into the percolator, leaving the flask in the top to drain. When the alcoholic filtrate has become somewhat concentrated, mix the drug remaining in the flask with 10 c.c. of 95 per cent. alcohol and pour the mixture into the percolator, draining the flask as before. Repeat the washing of the flask and the marc in the same manner until a portion of the percolate fails to show any opalescence on largely diluting with water. Concentrate the liquid at a gentle heat to a volume of about 10 c.c., remove the dish from the bath, and add water, a few drops at a time, to the warm extract, stirring with a glass rod, until the gum deposited by the concentrated, strongly alcoholic solution is redissolved and a clear, or nearly clear, fluid is obtained. Continue to add water in small portions, stirring thoroughly after each addition, up to a total quantity of 60 c.c., when the resin will have separated completely and may be collected in a mass under the aqueous solution, which should be quite clear. Put the dish on a boiling water-bath and heat with frequent stirring until the volume of liquid is reduced about one-third and the odor of alcohol has disappeared. Remove the dish from the bath, stir the liquid slowly so that the resin will collect, drawing any particles floating on the surface to one side, and decant the solution through a small filter. Cover the resin with 25 c.c. of water, return the dish to the bath, and, while the resin is hot and stringy, mix it thoroughly with the water. Remove from the bath, collect the resin as before, and decant the water through the filter. In like manner wash the resin a second time with 25 c.c. of water. Wash the edge of the filter with a little warm water and reject the several aqueous filtrates, first noting whether they are clear or, at most, show only that faint opalescence peculiar to solutions of gums. By means of a fine stream of hot alcohol from a wash-bottle, rinse the water remaining in the filter, together with any traces of resin, into the dish, then wash down the sides of the latter, finally warming and stirring until the resin is redissolved. Pour the alcoholic solution through the filter into a tared Erlenmeyer flask, wash the dish and filter carefully with hot alcohol, evaporate the solvent, and dry the resin to constant weight in a water-oven.

NOTES.—(1) The complete extraction of the cell-contents of a drug depends on the permeation by the solvent of every cell;

hence the necessity of first reducing the drug to a fine powder. If the sample of jalap consists of tubers, these are crushed in an iron mortar, then ground in a mill until the material passes through a No. 30 sieve, and finally pulverized by turning for several hours in a pebble mill.

(2) If strong alcohol is added directly to a finely powdered drug, the particles contract to such a degree that the menstruum percolates but slowly, if at all. When the powder is moistened with water as described above, it swells to nearly twice its original volume, the particles coalesce to form tiny granules which persist even after the addition of alcohol and heating, and the subsequent draining and washing of the drug in the percolator proceeds with great rapidity.

(3) The proportions of alcohol and water employed for the hot maceration are such as to produce a menstruum containing about 90 per cent. absolute alcohol, which appears to be a more efficient solvent than an alcohol of higher percentage.

(4) A pestle is easily made by heating the end of a glass rod 12 mm. in diameter quite hot, pressing firmly against a flat metal surface, then smoothing and rounding on a stone.

THE ASSAY PROCESSES OF THE U.S.P.[1]

By A. R. L. Dohme and H. Engelhardt.

On various occasions we have pointed out that several assay processes of the present U.S.P. are very much in need of being thoroughly revised, both because the methods are rather cumbersome, and the results are far from giving the true percentage of the active principle. Since the methods are going to be thoroughly discussed at the coming meeting of the A.Ph.A. we thought it necessary to again give our views in regard to the processes, although several points given here may have been discussed by us on previous occasions.

We still believe that the aliquot part method, when worked with precaution, gives more accurate results than the percolation method. The drug is more thoroughly exhausted by shaking with the men-

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[1] Read at the Boston meeting of the American Pharmaceutical Association, August, 1911.

struum than by percolating. A percolator is perhaps our most unscientific piece of apparatus. A channel might be formed in the packed drug, the parts adjoining this channel may be exhausted, while other parts of the drug come in contact with the menstruum only superficially. The method, besides that, is very tedious, especially when such a fine powder (No. 60) as prescribed by the U.S.P. is employed, and also requires a larger amount of menstruum for the exhaustion.

We, therefore, strongly recommend the adoption of the aliquot part method, having proven by numerous experiments that the results by this method compare favorably with those obtained by exhausting the drug completely by percolation.

For the final shaking out of the alkaloids, we recommend to use, whenever possible, simple menstrua, viz., ether or chloroform and not mixtures of both in various proportions. As a rule, simple menstrua are less liable to produce emulsions than mixtures, and the menstrua are more easily recovered for future use than mixtures, which always require tiresome adjusting.

For the extraction of the drugs, however, a mixture of ether-chloroform is to be preferred. Such a mixture seems to penetrate the cell-walls better than a simple menstruum, and consequently to extract the alkaloids more thoroughly. It is to be recommended to allow the drug to stand with the menstruum for at least one-quarter hour before adding the ammonia, as the results obtained by doing so are somewhat higher, in our opinion, than those obtained by adding ether-chloroform and ammonia to the drug together at once.

Whenever possible the alkaloids should be estimated by titration; only, in some cases when hydrolysis is liable to take place, as in aconite, coca leaves, etc., a check by gravimetric estimation might be of advantage.

Of all the indicators for alkaloids, we have found cochineal to be the best, since only in titrating the alkaloids of ipecac is any difficulty experienced with this indicator. Iodeosin, at present used in the U.S.P., is rather unreliable since the aqueous liquid is not always colored red when the end point is reached, but at times a red scum is formed at the contact of the two layers, the color of this scum increasing in intensity with the addition of the alkali. It is difficult to judge, in case this happens, when the end point is reached.

In regard to the various drugs and the galenical preparations thereof, we beg to offer the following suggestions:

Aconite Root.—To avoid hydrolysis as much as possible, ammonia might be replaced by sodium carbonate or bicarbonate solution. The present process is very tiresome; only in the case of a larger dilution can a somewhat rapid filtration be effected. Keller's aliquot part process, using ether-chloroform and sodium bicarbonate for extracting the drug, and ether alone for the final extraction of the alkaloid, after having made the acid solution alkaline with sodium bicarbonate, gives very good results. The wording, "not less than 0.5 per cent. of aconitine," should be replaced by "not less than 0.5 per cent. of ether soluble alkaloids," since the residue, although it consists for the greatest part of true aconitine, is always contaminated with other basic substances. The Squibb's test has been found to be too much dependent on individuality.

Extract Aconite.—No matter how carefully this extract is prepared, a deterioration of the alkaloids is liable to take place, and the physiological strength consequently is largely reduced. Extract aconite should never be prepared. In assaying extract of aconite, the following simple process gives rather accurate results: Dissolve the extract (2 grams) in 10 c.c. of dilute alcohol, transfer the solution to a separator, make alkaline with sodium bicarbonate solution and shake out with several portions of ether. From the ethereal solution the alkaloids are extracted by shaking with several portions of acidulated water, and from the latter, after making alkaline with sodium bicarbonate, the alkaloids are removed by shaking with several portions of ether. From the etheral solutions, after filtering to remove any suspended bicarbonate, the ether is distilled off, etc.

Fluidextact Aconite.—Ten c.c. are transferred to a separator, made alkaline with sodium bicarbonate, and then assayed as just given.

Tincture Aconite.—One hundred c.c. of the tincture are evaporated at a temperature not exceeding 60° C., the residue taken up in 10 c.c. of dilute alcohol, and this solution assayed as given under extract.

Aqua Hydrogenii Dioxidi.—The method for determining the acidity should be revised. By evaporating 25 c.c. of hydrogen peroxide solution to 10 c.c. in the presence of 5 c.c. of N/10 potassium hydroxide solution, not all the hydrogen peroxide is destroyed.

This can be effected only by evaporating the solution in a platinum dish or by adding a suitable catalyzer, such as platinum black, etc.

Asafœtida.—Owing to the scarcity of this article, it would be advisable to decrease the percentage of alcohol soluble matter, and to increase the allowable percentage of ash.

Aspidium.—The activity of this drug depends almost entirely on those substances present in what is generally termed "crude filicin." A reliable method has been worked out for determining crude filicin. The macroscopic requirements given in the present U.S.P. will be met by a physiologically inactive drug also.

Belladonna Root and Leaves.—The assay process adopted for the new U.S.P., viz., the aliquot part method, has a decided advantage over the present process, and gives very satisfactory results.

Fluidextract and Extract of Belladonna.—The assay processes for these preparations are satisfactory. It is, however, advisable to increase the amounts of both the immiscible solvents and the acidulated water.

Cantharis and Its Preparations.—These should be assayed. Several reliable methods have recently been published. A suitable menstruum for preparing the tincture should also be looked for, as by the present menstruum only about 50 per cent. of the cantharidin is extracted from the drug when used in the proportion 1 : 1.

Capsicum.—We have met with several specimens of inferior capsicum. Why not give and estimate the percentage of oleoresin?

Cinchona.—For the U.S.P. IX, unfortunately, an assay process has been proposed, which is similar to the one now official, differing from it only by the larger amount of menstruum taken for extracting the alkaloids from the drug. Although this is a step in the right direction, we doubt very much whether the increased quantity of menstruum will hold in solution the alkaloids from high-grade drugs. The Fromme process, depending on the breaking up of the cells by the use of hydrochloric acid, has always given us satisfactory results. It is a short one, and a determination can easily be carried out in two hours. That such a process is of great importance to chemists who have to make a dozen or more cinchona assays at the same time (as in our laboratory, when numerous samples for purchasing the drug are submitted) is obvious. We wish to mention again that the alkaloidal residue should be dried at a temperature not exceeding 60° to 70° C., as otherwise it is strongly discolored. Any traces of chloroform should be driven

off by treating the residue twice or three times with ether. In our laboratory, we invariably control the gravimetric results by titration, because the alkaloidal residue very frequently includes waxy and other substances, which naturally increase the weight. The titration when carried out strictly according to Panchaud's direction, is not at all difficult.

Coca.—Here also the percolation process should be abandoned in the assay method. Keller's method, using plain ether, gives very satisfactory results. In case emulsions occur, which frequently takes place on account of the large amount of mucilaginous matter in the drug, tragacanth should be used for breaking up the emulsions.

Cochineal.—It is advisable to include in the U.S.P. a determination of the color strength of the drug, also an estimation of the moisture.

Colchicum Seed and Corm.—We have pointed out on various occasions that the results obtained by the present assay methods are absolutely wrong, that the residue calculated as colchicine contains only about 50 per cent. of the alkaloid. The assay processes should be thoroughly revised. Dr. A. B. Lyons has given valuable information in what way these processes could be improved. For the estimation of pure colchicine in the alkaloidal residue, several methods are available also. We do not care to go into details about these improvements, since we have given a compilation of them some time ago.

Conium Seed.—The assay method for this drug also should be revised. It is very cumbersome and could easily be replaced by a more expeditious process.

Conium Leaves.—This drug, although not official, should never be used. All the samples submitted to this laboratory for examination were almost void of coniine.

Cubebs.—An estimation of and requirements for the percentage of oleoresin should be given. Cubebs vary considerably in the amount of oleoresin.

Emplastrum Belladonnæ.—A few slight modifications of this assay process have recently been recommended. The process, however, we find works very well.

Ergot.—On various occasions we have mentioned a simple process to estimate the approximate amount of cornutine present in the drug. If it can be proven beyond doubt that the percentage of cornutine is in proportion to the physiological activity, this test should be adopted for the U.S.P.

Ferrum Reductum.—The assay process could be improved on.

Gelsemium and Its Preparations.—Assay processes for these substances have been recommended on various occasions. We believe, however, that such a process is only of relative value as long as the proportion of the active substance to the inactive is not known in the residue determined as total alkaloids. Quite recently a good deal of light has been thrown on the constituents of gelsemium and possibly in the near future an assay process based on the estimation of the active principle alone will be worked out.

Glandulæ Suprarenales et Thyroideæ.—Colorimetric or chemical estimation of the active principles is desirable.

Granatum.—The total alkaloids in pomegranate bark can easily be estimated.

Guarana and Its Preparations.—The assay processes are good.

Hydrastis and Its Preparations.—The amount of golden seal taken for the assay is entirely too large considering the high percentage of hydrastine in the drug. There is no reason why the assay of the fluidextract should not be based on the same principle as the assay of the drug.

Hyoscyamus and Its Preparations.—All that is said about Belladonna applies to these products also.

Ipecacuanha and Its Preparations.—The amount of drug prescribed for the assay process should be reduced considerably, say to about 6 grams. The assay process otherwise is satisfactory. We have pointed out above that the titration of the alkaloidal residue is somewhat difficult, and it would be desirable to try other indicators which might prove to be more satisfactory.

Jalap.—A shorter process depending on the exhaustion of the root with hot alcohol and taking, after cooling and readjusting the weight, an aliquot part has been recommended by us on a former occasion. In connection with this drug it may be said that the quality of the various samples and shipments during the last twelve months was superior to that in previous years. Would it not be advisable to control the galenical preparations of jalap by simple assay processes?

Kola and Its Preparations.—These should be assayed by a process similar to that given for guarana. To estimate the amount of theobromine, acid instead of water has to be used for extracting the alkaloids from the chloroformic solution.

Maltum and Extractum Malti.—It is advisable to give assay

processes for the determination of maltose and diastatic power. We have met with numerous samples of malt which were deficient in both respects.

Nux Vomica and Its Preparations.—Keller's aliquot part method, using ether and chloroform, gives fairly good results; it must, however, be admitted that the results obtained by using the U.S.P. menstruum are slightly higher. The amount of powdered drug can be reduced on account of the high percentage of alkaloids in the drug. It is to be regretted that the U.S.P. IX again shall adopt a method for determining the strychnine. The present official method and the numerous modifications thereof give fairly accurate results only in the hands of experienced workers. We doubt very much that the variation of the proportion of strychnine and brucine in the drug is greater than the variation obtained by assaying the same drug by various chemists. Only such methods should be adopted in the U.S.P. which are simple and give fairly accurate results, and not such ones which require much ability and experience. The U.S.P. is not written for experienced chemists, such as are generally found in the laboratories of the large wholesale houses, but for the retail pharmacist also, who very seldom has and will have a thorough experience in assaying drugs. We have mentioned on other occasions that of all the pharmacopœias only the English directs the strychnine to be estimated, and this is done by a method which is still inferior to the old Gerock method and its modifications. We are afraid that by adopting the strychnine determination much trouble and numerous litigations will be caused. If it is important to determine the strychnine alone, why has not a process for doing so been adopted by the Swiss, German, etc., pharmacopœias, which without doubt are up-to-date works? Is brucine therapeutically absolutely inert, and can it be entirely neglected? In our opinion, the determination of the total alkaloids (which by no means is such a very simple one, on account of the ammonia bases and the soap which are liable to be formed during the assay process) is a better criterion for the quality of the drug, than an unreliable and incorrect estimation of the strychnine alone.

Extract Nucis Vomicæ.—The easiest way of assaying this extract is to convert the extract into a fluidextract by dissolving in diluted alcohol, rendering the solution alkaline with ammonia water, shaking out with several portions of chloroform, etc.

Fluidextractum and Tinctura Nucis Vomicæ.—Evaporate the

quantity prescribed for the assay to dryness, take up residue in dilute alcohol, and proceed as just given.

Opium.—In regard to this drug, we wish to refer to an article submitted to the A.Ph.A. (Proc. A.Ph.A., 1910, page 829) a year ago. There is no doubt that by the present official process almost the entire morphine contained in the drug is obtained, although Debourdeaux, *Journ. de Pharm. et Chem.*, vii, iv, 68, claims that by further exhaustion with water, still more morphine can be exhausted. He also claims that if the crude morphine, as obtained by the U.S.P. process, is not washed thoroughly, lime-water soluble substances are determined as morphine, rendering the percentage of the latter too high. We have obtained very good results with the present method; we think, however, that a shortening of the process would be desirable.

Extract Opium and Tincture Opium.—The assay methods work satisfactorily.

Pancreatin.—For the assay process the use of potato starch should be recommended. The milk test is unreliable and should be deleted.

Pepsin.—We have at times experienced considerable trouble with the assay process, which apparently was due to the age of the eggs. Recently we have only used eggs from 5 to 10 days old, and have obtained with such material rather concordant results. At the Indianapolis meeting of the Am. Chem. Soc. a paper will be read dealing with the use of dry egg albumin in the assay process of pepsin. If the results obtained by using dry albumin are encouraging, this modification should certainly be tried by the Revision Committee. Dry albumin can more easily be obtained in a uniform quality than fresh albumin, which contains a varying amount of water, according to the age of the eggs.

Physostigma and Its Preparations.—Slight modifications as to the quantities of immiscible solvent and acidulated water should be made.

Extractum Physostigmatis.—The use of sand and evaporation to dryness are to be avoided. We prefer to use powdered glass and to evaporate the liquid until the alcohol is expelled. Such a moist mass can be transferred to a bottle much easier than the hard mass obtained by the official process. Results just as accurate can be obtained by converting the solid extract into a fluidextract by dis-

solving it in dilute alcohol, rendering alkaline with sodium bicarbonate, shaking out with ether, etc.

Fluidextractum and Tinctura Physostigmatis.—The modifications just mentioned apply to the assay of these preparations also.

Pilocarpus and Its Preparations.—Replace the percolation process in the assay method by the aliquot part method. In case emulsions should be formed, use tragacanth for breaking up emulsions.

Fluidextractum and Extractum Pilocarpi.—The modifications suggested under physostigma apply to the assay processes of these preparations also. Fluidextract of Pilocarpus can be assayed by shaking out directly with chloroform after making alkaline with ammonia. Emulsions which are liable to be formed can be avoided by using a large amount of chloroform.

Piper.—The percentage of oleoresin should be determined.

Podophyllum.—Mandrake with less than 4 or 4.5 per cent. of resin is frequently met with on the market. An assay process for this drug therefore seems necessary.

Fluidextractum Podophylli.—The percentage of podophyllin should be determined.

Sanguinaria.—An estimation of the total alkaloids of blood-root might be valuable, although such a determination possibly does not indicate the therapeutic value of the drug.

Scopola and Its Preparations.—All that is said in regard to belladonna applies to this drug also.

Sinapis.—An estimation of allyl-iso-thiocyanate can be recommended.

Stramonium and Its Preparations.—See modifications recommended under belladonna.

Strophanthus.—There is no reason why this potent drug should not be assayed. A reliable process has been worked out.

Veratrum.—An estimation of the total alkaloids has been recommended on various occasions.

In conclusion we wish to say again that we hope that in the U.S.P. IX such assay methods will be adopted which are easily carried out with the simplest apparatus, and in as short a time as possible, which, however, give at the same time reliable results, not theoretically accurate but practically accurate.

THE CULTIVATION OF MEDICINAL PLANTS AT THE COLLEGE OF PHARMACY OF THE UNIVERSITY OF MINNESOTA.[1]

By Edwin L. Newcomb, in Charge Department of Pharmacognosy.

The Medicinal Plant Garden of the College of Pharmacy of the University of Minnesota was designed primarily to facilitate and make more comprehensive the instruction in Pharmaceutical Botany and Pharmacognosy. It furnishes one of the essential means of giving instruction pertaining to the vegetable drugs or their preparations. The proper development of such a garden gives the student an excellent idea of the origin of vegetable drugs and not infrequently is the cause of the production of botanical enthusiasts, which all pharmacists should in reality be. The teaching of pharmaceutical botany and pharmacognosy without a medicinal plant garden is not comparable in efficiency with that supported by an adequate drug garden. With such an accessory the students are soon impressed with the distinguishing characters of such families of plants as the Compositæ, Solanaceæ, Umbelliferæ, etc., and they are quickly able to identify such plants as Digitalis purpurea, Verbascum thapsus, Inula helenium, Hyoscyamus niger, Atropa Belladonna, etc.

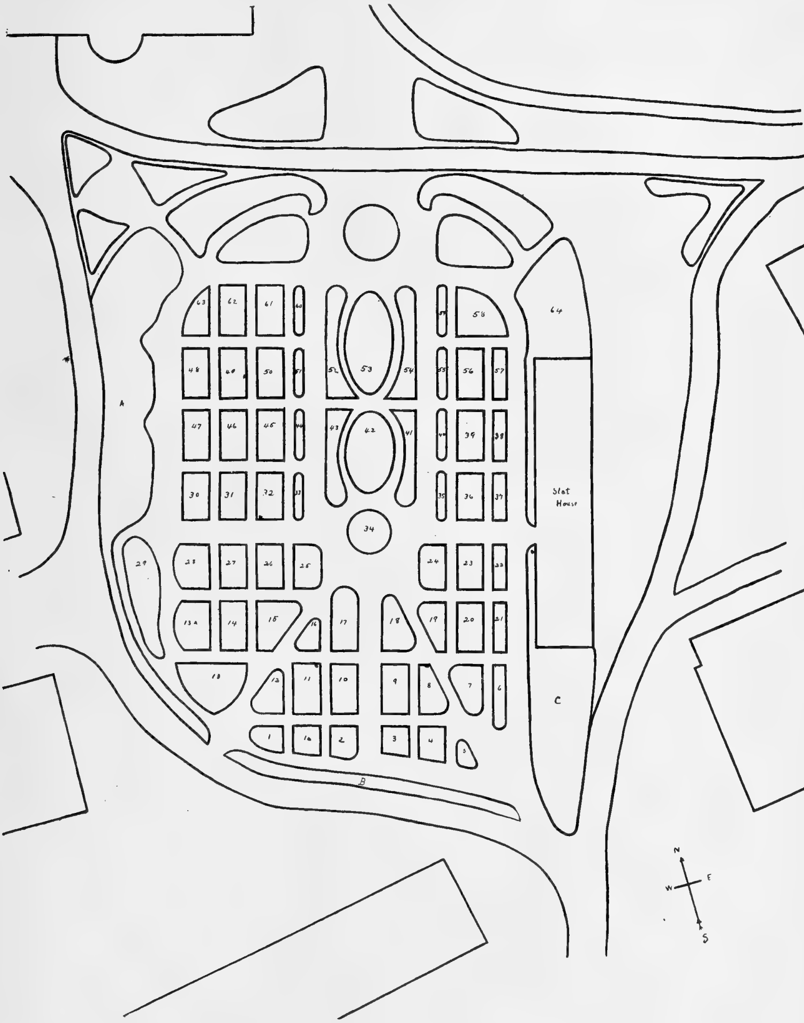
While it is true that the growing plant which ultimately yields the drug usually presents an entirely different appearance from the drug itself, this need not mitigate against or complicate the instruction. It rather facilitates it, for a thorough knowledge of the characters of the plant will insure a quick eye to identify the cured product or to detect inferiority in it, and the familiarity with the plants soon removes most trouble with nomenclature.

With the decided advantages which such facilities afford in giving instruction in pharmacy courses, it seems strange that so few colleges in this country have up to this time established independent medicinal plant gardens. A number of institutions are so situated that they have access to botanic gardens where many medicinal plants may be found growing. This association, good as it may be, does not meet the urgent need of a medicinal plant garden

[1] Read at the fifty-ninth annual meeting of the American Pharmaceutical Association, Boston, August 17, 1911.

in close proximity to and under the direct supervision of the college itself.

It is now nineteen years ago that Dean Wulling, realizing the



Plan of the Medicinal Plant Garden of the College of Pharmacy of the University of Minnesota.

need of such a garden, asked the Board of Regents of the University for a tract of ground and funds to establish medicinal plant cultivation. About fourteen years ago a plot of ground was granted, but no

funds were available and hence nothing apparent was accomplished at this time at the college, but Dean Wulling started a garden on a small scale at his home, which, however, he soon after abandoned principally because of lack of time and area. In the fall of 1910 an appropriation was secured for the establishing of a medicinal plant garden and late this spring the ground which had been granted some fourteen years ago was plowed for the College of Pharmacy and actual work begun.

The garden is admirably located and of about forty thousand square feet in area immediately adjoining the building occupied by the College of Pharmacy. It represents part of the University campus which some time ago was a shallow basin, but which has been filled in during the past few years. On this account the soil is quite varied, consisting mostly of light sandy loam with a coating of peat. The plot is surrounded on all sides by buildings which afford considerable protection. After the ground had been plowed and thoroughly harrowed, it was staked out into plots of convenient size and shape, for the most part 10 x 18 feet. A few beds of more ornamental design were prepared as the garden was to occupy a rather conspicuous location on the campus.

The question which has frequently been asked in connection with medicinal plant cultivation is, "Where can the seed or plants be obtained to make the start?" Many of our medicinal plants are used as ornamentals and hence American and European seed dealers are able to supply a certain amount of the desired seeds. In case the drug consists of the seed or fruit this, if not too old, may furnish a very valuable means of starting the work of propagation. Samples were taken from the drug collections at the College of Pharmacy of some fifty-eight different drugs and of these thirty germinated, giving in a short time a supply of plants yielding these drugs. This experiment disclosed a rather valuable test for the identification of certain seed drugs. A sample of Delphinium consolida on two germination tests showed the presence of ten per cent. of the seed of an entirely different plant. So close was the similarity of the two seeds that the adulterant would go undetected unless a microscopic examination was resorted to. The reason for the germination of only fifty per cent. of the various seeds tested was probably due to either or both of two causes: first, the age of the seed and second, injury to the vitality in preparation of the drug.

Among the seed taken from the drug collection which grew

and furnished strong plants may be mentioned those of Atropa belladonna, Delphinium consolida, Conium maculatum, Pimpinella anisum, Coriandrum Sativum and others from the Umbelliferæ Delphinium Staphisagria, Citrullus Colocynthis, Datura stramonium, Hyoscyamus niger and Lobelia inflate.

Seeds of the above plants and some fifty others were purchased from New York seed dealers and started in the greenhouse about February 17. Among the seed shown at this time were those of the following plants: Inula helenium, Capsicum spec., Arnica Montana, Glycyrrhiza glabra, Cytissus scoparius, Carthamus tinctoria, Lavandula spec., Passiflora incarnata, Matricaria Chamomilla, Coix lachryma, Datura metelloides, Rheum palmatum Ricinus spec., twelve varieties of Digitalis and many others.

Most of the seed germinated in from one to two weeks and the method of handling the seedlings being much the same in each case, a description is here given of Digitalis.

After carefully preparing the soil which was of good rich light moist loam containing a large amount of well-rotted sod and leaf mould, it was placed in four- or five-inch flower-pots supplied with a few pieces of broken pot for drainage. The soil should be lightly pressed down so that the surface is smooth and quite firm. The seed were then spread over this prepared surface and covered with the same soil, to which about forty per cent. of sand had been added. The seeded pots thus prepared were thoroughly watered with a rubber bulb sprinkler which does not wash the soil. Each pot was covered with a plate of window glass to retain the moisture. In the preparation of the soil it is important to select that which is as free from weed seeds as possible.

Digitalis lutea, Digitalis lanata, Digitalis grandiflora and Digitalis ferruginea gigantes required from thirteen to fifteen days to come up, while Digitalis purpurea rosea, Digitalis purpurea maculata superba, Digitalis purpurea gloxiniæflora alba, Digitalis purpurea monstrosa and Digitalis purpurea alba all germinated in from nine to thirteen days. In from two to three weeks the plantlets were well started, having one or two pairs of leaves. At this time they were transplanted into flats (shallow boxes about three inches deep and preferably eighteen by twenty-four inches in area). The same rich finely pulverized soil was used here as in the planting of the seed. The plants were put about two inches apart each kind in a separate flat and the soil firmly pressed about the roots. When

the plants became crowded in the flats they were transplanted into two and one-half or three-inch pots.

The next step was that of hardening off the plants before final planting. This was done by placing them outside in cold frames for the early part of May, glass being kept over them all the time for the first few days and then gradually withdrawn. The plots in the garden were worked over with a spading fork and the plants put in rows eighteen inches apart each way. About twelve hundred plants of the different species of Digitalis have been handled in the above described manner, the outside planting taking place from May 20 to June 20. The plants in the first beds put out have made a remarkable growth and the ground is covered with the beautiful rich green foliage.

In addition to the large number of plants started from seed, some plants were purchased, representing trees, shrubbery and hardy perennials from which drugs are obtained. The seed of over four hundred medicinal plants were imported and a large number of these are under cultivation, others are being put in as rapidly as the ground can be prepared.

A hedge of Rhamnus catharticus has been planted on the west and south sides of the garden. Within this are border beds filled with more or less tall growing annuals or perennials as Inula Helenium, Ricinus species, Hibiscus militaris, Borago officinalis, Atropa Belladonna, Martynia proboscidia, Datura Stramonium and Helianthus annus. At the north end the border widens out into a broad plot which is filled with Papaverum somniferum, Salvia officinalis, Nicotiana Tabacum, Salpiglossis, Canna, Thymus vulgaris, Lavandula vera and others. At intervals of twenty feet along the border such trees as Ulmus fulva, Xanthoxylum Americanum, Juglans nigra, Salix alba, Quercus alba, etc., have been planted. These outside beds are bordered with Digitalis spec., Cineraria maritima, Dianthus spec., Impatiens balsamina and Antirrhinum majus.

A large plot has been laid out at the south end of the slathouse and here may be found growing an interesting group of evergreens and other plants closely related botanically as Larix Europœa and Salisburia adiantifolia, the Japanese Ginkgo tree. Between the trees a collection of the plants which yield our common pot herbs have been temporarily located, including Ocimum Basilicum

Hyssopus officinalis, Melissa officinalis, Majoranum hortense, Origanum vulgare, Tanacetum vulgare, etc. Along the south side of the slathouse various varieties of Vitis vinifera have been put in to afford additional shade. Between these Citrullus Colocynthis was planted.

The slathouse, a structure one hundred feet long, twenty feet wide and seven and one-half feet high, extends along the east side. A collection of shade loving plants has already been obtained, including Cimicifuga racemosa, Podophyllum peltatum, Hydrastis canadensis, Geranium maculatum, Sanguinaria canadensis, Spigelia marilandica, Aspidium species, Cypripedium spec., and many others. A long bed is laid out along the front of the house and here different species of the following genera have been planted: Luffa, Momordica, Citrullus, Convolvulus, Bryonia, Cucurbita and Cucumis. In addition to these climbers, such perennials as Clematis, Humulus, Ampelopsis, Solanum, Wistaria, Aristolochia and Pueraria species are to be found. The entire length of the bed is bordered with Digitalis species and there is also a fine display of Cannabis gigantea, Cannabis american, Fœniculum vulgare and Zea Mays varieties.

The largest portion of the garden is laid out into the rectangular plots previously referred to. Of these the following are deserving of special mention:

Plot No. 4 is planted with Conium maculatum. This plant has done remarkably well. Several of the specimens now in blossom have attained a height of over four feet.

Plot No. 6 contains Ricinus communis var. minor and Ricinus communis var. major as well as a number of other species. The seed sold as drug often appears to be a mixture of seed from the different species of Ricinus.

Plots Nos. 8, 12, 13, 16, 28, 48, 49, 61 and 62 are filled with different varieties and species of Digitalis and it is hoped that some work can soon be done concerning the factors which influence the potency of the official drug.

Plot No. 14 contains Aconitum Napellus, A. Lycotonum and A. Fischerii, also Delphinium Staphisagria and other species of Delphinium.

In Plot No. 17 may be found capsicum frutescens and other species of capsicum.

Plot. No. 20.—Sinapis nigra and Sinapis alba.

Plot No. 24.—Coriandrum sativum, the drug purchased in the open market was used to plant this bed. The plants have made a fine growth and give promise of fruiting long before frost.

Calendula officinalis fills No. 25, a plant exceedingly easy of cultivation and producing a profuse number of flowers.

Plot No. 26 contains Matricaria Chamomilla. This bed is now a mass of the beautiful little white daisies and, like calendula, is very easy to grow.

In Plot No. 27 are twelve plants of Datura metelloides, which cover the entire 160 square feet devoted to them and present a magnificent sight in the evening when their large pure white odorous flowers expand.

Nicotiana repanda yielding Havana tobacco and N. Tabacum, yielding the so-called Pennsylvania and other commercial varieties of tobacco are growing luxuriantly in Plot. No. 30.

A fine group of Atropa belladonna seedlings is found in Plot No. 31, as well as a few flowering plants.

Plot No. 36 contains such Xerophytic plants as Aloe spec., Agave Americana, Cactus grandiflora and Euphrobia pilulifera, the border consisting of Echeveria spec.

Plots Nos. 39 and 56 are filled with such cereal yielding plants as Avena sativa, Hordeum sativum, Triticum sativum and Secale cereale.

Three varieties of Hyoscyamus are being studied, namely, H. niger, H. albus, and H. pictus.

Several plots throughout the garden were assigned to drug yielding shrubs. Some fifty of these have been planted, including Viburnum opulus and other species, Chionanthus Virginia, Hydrangea arborescens, Berberis vulgaris, Cornus stolonifera, Sambucus canadensis, S. nigra, S. pubens, Prunus serotina, Prunus Virginiana and Euonymus atropurpureus. Between the shrubs hardy perennials have been planted, such as Monarda species, Helenium autumnale, Iris spec., yielding Orris, Phlox spec., Pæonia officinalis, Yucca filamentosa, etc.

On five of the plots cold frames covered with sash were constructed. Many plants were started in these and they will be used again this fall for giving slight protection to certain plants during the winter.

Over one-half of the medicinal plants yielding official drugs are already under cultivation and more are being continually added.

Of those which do not yield official drugs the number is much larger and it is planned to add representative specimens as rapidly as possible of all drug yielding plants, some of which necessarily must be conserved in the greenhouse.

The general plan in developing the garden was to keep different species of plants belonging to the same family in beds of close proximity. This was followed out to a certain extent, but until soil conditions can be produced as desired in each plot the plan will not be entirely feasible. Such an association of plants greatly enhances the value of the garden in giving instruction in pharmaceutical botany.

The effect of different soils, moisture, etc., on the constituents of certain plants is to be carefully observed and it is hoped that some valuable pharmaco-physiologic work can soon be accomplished.

NEW ESSENTIAL OILS.[1]

Oil of Chamæcyparis Lawsoniana.—More than 20 years ago[2] we reported on the oil of the genus *Chamæcyparis* (N. O. Coniferæ), the sample then referred to being the product of *Chamæcyparis obtusa* Endl., a native of Japan. We are now in a position to describe the oil of a second species, *Chamæcyparis Lawsoniana* Parl. (*Cupressus Lawsoniana* A. Murr.), a stately coniferous tree, often found in German gardens. This oil was distilled by ourselves. The distilling material, which came from Holstein, yielded about 1 per cent. of a lemon-yellow oil of an odor reminding of oil of savin or of cypress. Its other properties were as follows: $d_{15°}$ 0,9308, $\alpha_D + 23° 48'$, $n_{D_{20°}}$ 1,48844, acid no. 3,7, ester no. 61,6, ester no. after acetylation 78,8, soluble in ½ its vol. of 90 per cent. alcohol, with 1 to 3 vols. passing turbidity. With bisulphite we succeeded in isolating small quantities of an aldehyde which, judging by its odor, was perhaps identical with laurinic aldehyde.

Camphor from Cinnamomum Glanduliferum.—R. S. Pearson, of Dehra Dun, has obtained from the leaves of *Cinnamomum glanduliferum,* a laurel-tree growing in the districts south of the Himalayas, a camphor which must probably be regarded as identical with the Japanese commercial product. A sample of the crude product, which has been sent to us by Mr. Pearson, possessed a m.p. of 175°, which was raised to 176° after recrystallization from dilute alcohol.

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[1] From Semi-Annual Report of Schimmel & Co. (Fritzsche Brothers), October, 1910.

[2] Schimmel's Report, 1889.

The sp. rotation of the purified camphor in 55,55 per cent. alcoholic solution (90 per cent.) was $[\alpha]_D + 46{,}32°$; in a 43,91 per cent. solution of xylene $[\alpha]_D + 49{,}12°$, falling to $[\alpha]_D + 48{,}72°$ after the solution had been allowed to stand for 10 days. The oxime melted at 118° and, as was to be expected, rotated in the opposite direction, that is to say, to the left. When boiled with acetic anhydride no alcoholic constituent, such as borneol, could be detected; the crude product, therefore, consisted only of d-camphor.

Oil of Dacrydium Franklinii.—A distillate obtained from the wood of *Dacrydium Franklinii* Hook. f. (*D. huonense* A. Cunn.) has been sent to us from Melbourne, Victoria. The tree, which belongs to the Coniferæ, is known there as "Huon Tree." The oil was of a pale yellow color and had a pronounced odor of methyl eugenol, which, in fact, forms its principal constituent. $d_{15°}$ 1,0443; $\alpha_D + 0° 6'$; $n_{D_{20°}}$ 1,53287; acid no. 0,9; ester no. 1,5; soluble in 5,2 vols. and more of 60 per cent. alcohol; the dilute solution showed a faint opalescence. In distilling, the greater part of the oil passed over between 251 and 253° [754 mm. (98 to 100° at 2 to 3 mm.)] and proved to be methyl eugenol, which was identified by conversion into veratric acid (m. p. 179 to 180). The oil also contains traces of eugenol (benzoyl compound, m. p. 70°). The methoxyl determination gave the high methyl value of 164,3, from which the methyl eugenol content was calculated as 97,5 per cent. but in reality it is probably a little less.

Oil of Eugenia Apiculata.—In Chili a drug known locally as "arrayan" is used in diarrhœa and in affections of the lungs, for which purposes it is said to enjoy a high repute among the natives. According to Tunmann[3] it consists of the young leaves, about 15 mm. long and 10 mm. broad, of a small tree of the family of the Myrtaceæ, *Eugenia apiculata* D. C. In addition to a glucoside-like tanning principle the leaves contain an essential oil, to which their medicinal virtues are specially attributed. We have worked up a parcel of these leaves, which yielded 1,27 per cent. of a brown oil, with an odor resembling that of oil of myrtle, and possessing the following constants: $d_{15°}$ 0,8920, $\alpha_D + 12° 40'$, $n_{D_{20°}}$ 1,47821, acid no. 5,5, ester no. 25,8, ester no. after acetylation 65,3, soluble in 0,5 vol. and more of 90 per cent. alcohol, paraffin being separated out when the solution is diluted; the oil is not soluble in 10 vols. 80 per cent. alcohol.

Oil of Perilla Nankinensis.—*Perilla nankinensis* Decne. (*Perilla*

[3] *Pharm. Zentralb.*, **50** (1909), 887.

arguta Benth.; *Ocimum crispum* Thunb., N. O. Labiatæ), which is known in Japan as "*Shiso*" and of which the leaves are used as a vegetable and a spice, contains an essential oil of which we recently received a sample from Yokohama. The oil was mobile, pale-yellow to greenish, of a peculiar hay-like odor, and possessed the following constants: $d_{15°}$ 0,9265, $a_D - 90°$, $n_{D_{20°}}$ 1,49835, soluble in 0,3 vols. and more of 90 per cent. alcohol. It reacted both with acid and with neutral sodium bisulphite, 50 per cent. of an aldehyde being obtainable by this reaction. The odor of the aldehyde reminded somewhat of cuminic aldehyde, but in its properties it differed altogether from that body, as was evident, for example, from the fact that it reacted with neutral bisulphite of sodium. A sample was carefully purified from the sulphite compound and distilled first with steam and afterwards *in vacuo* under 4,5 mm. press. This sample was found to possess the following constants: b. p. 91° (4,5 mm.), 104° (9 mm.), 235 to 237° (750 mm.), $d_{20°}$ 0,9645, $d_{15°}$ 0,9685, $a_D - 146°$, $[a]_D -$ 150,7°, $n_{D_{20°}}$ 1,50693. The oxime, which was also lævorotatory, melted at 102°, the phenylhydrazone at 107.5°. The aldehyde was oxidizable into the corresponding acid both by moist oxide of silver and with Beckmann's chromic acid solution.[4] It is almost insoluble in water but readily soluble in almost all organic solvents. Recrystallized from dilute alcohol it forms delicate white scales, m. p. 130°. So far, our attempts to elucidate the chemical constitution of the aldehyde have led to no result.

In connection with the above we wish to make a brief reference to an oil which is of special interest because it contains a dextrorotatory variety of the aldehyde described above. A sample of wood which was sent to us some time ago under the name of "spurious camphor wood" (*faux camphrier*), but to the botanical derivation of which we were unfortunately not able to obtain any clue, yielded upon distillation 2,06 per cent. of a pale yellow oil with an odor similar to that of the oil from *Perilla nankinensis* just referred to, $d_{15°}$ 0,9580; $a_D + 98°\ 10'$; $n_{D_{20°}}$ 1,49695; soluble in 2,5 vols. and more of 70 per cent. alcohol. The oil contained 75 per cent. of an aldehyde which reacted both with neutral and with acid sodium bisulphite, and otherwise agreed in every respect with the aldehyde contained in the oil of *Perilla nankinensis,* except that it rotated in the opposite direction. The properties of the aldehyde isolated with sodium bisulphite were as follows: b. p. 234 to 236° (743 mm.), 98 to 100° (7 mm.), $d_{15°}$ 0.9730, $a_D + 137°\ 40'$, $n_{D_{20°}}$ 1,50802. The

[4] *Liebig's Annalen,* **250** (1889), 325.

aldehyde was evidently not yet quite pure, which may explain the slight discrepancies between the two aldehydes. The oxime, like that of the first aldehyde, melted at 101 to 102°, the phenylhydrazone at 107 to 108°, an inactive mixture of the two aldehydes gave rise to derivatives showing the same melting points. The portions of the oil which did not react with bisulphite contained small proportions of cineol, which were isolated by means of the resorcinol compound.

Oil of Thymbra Spicata.—The labiate *Thymbra spicata* L., a native of Greece and Asia Minor, is a shrub-like plant closely allied to the genus *Thymus*. We have distilled some of this herb, which came from Smyrna, and obtained a yield of 1,5 per cent. of a yellowish oil with an odor reminding of thyme and origanum, and containing about 66 per cent. of carvacrol. The oil had the following constants: d_{15° 0,9460, $\alpha_D + 0$, $n_{D_{20^\circ}}$ 1,50675; soluble in 3,5 vols. of 70 per cent. alcohol.

Oil of Xanthoxylum Alatum.—From London we received under the name of "Chinese Wild Pepper" the fruit of *Xanthoxylum alatum Roxb.*, a shrub belonging to the Rutaceæ, which occurs in the mountains of Northern Bengal as well as in China. Upon distillation the fruit yielded 3,7 per cent. of a lemon-yellow oil with a peculiar odor, reminding of oil of water-fennel. Continued distillation yielded, in addition, 0,9 per cent. of a crystalline substance. We were compelled to abandon the attempt to dissolve this substance in the oil in the proportion indicated, because the bulk of the solid constituents again separated out even at a temperature of 25 to 30°. The properties of the oil and of the solid substance were therefore determined separately. The oil behaved as follows: d_{15° 0,8653, $\alpha_D - 23^\circ\ 35'$, $n_{D_{20^\circ}}$ 1,48131, acid no. 9,9, ester no. 10,3, ester no. after acetyl. 33,6, soluble in 2,6 vols. and more of 90 per cent. alcohol. According to these analytical values the oil appears to consist chiefly of hydrocarbons, the nature of which remains to be elucidated by further investigation. The odor suggests the presence of phellandrene.

The solid substance which was obtained in the process of distillation, after being twice recrystallized from alcohol, presented colorless, odorless, optically inactive needles or leaflets, m. p. 83°. It was very readily soluble in ether, chloroform, and acetone, a little less readily in alcohol, benzene, and light petroleum (all three of which solvents are very suitable for recrystallizing the body), and

was insoluble in water. The substance is not an acid, it appears rather to be a phenol or lactone-like compound, as is evident from the fact that it does not react with solutions of alkaline carbonates, while it does react with those of caustic alkalies, from which latter it is again separated out by acidulation. Although when heated with benzoyl chloride it reacted violently, the yield of the resulting benzoyl compound was only slight, the greater part of the compound having remained intact. After repeated recrystallization from alcohol the benzoyl compound formed stout crystals, melting at 89°.

Dr. A. J. Ultée, of Salatiga, Java, has recently sent us two samples of essential oils which we desire to describe here only briefly, as a detailed publication concerning their composition has been promised by Dr. Ultée himself.

Oil of Alpinia Galanga Willd.—(N. O. Zingiberaceæ). This oil was of a lemon-yellow color and possessed a peculiar, strongly aromatic odor. Its constants were as follows: d_{15° 0,9847, α_D + 4° 20′, $n_{D_{20^\circ}}$ 1,51638, acid no. 1,8, ester no. 145,6, soluble in its own vol. of 80 per cent. alcohol, opalescence ensuing upon the addition of 3 vols. According to Dr. Ultée, the oil contains pinene, cineol, camphor, and methyl cinnamate. The ester number of the oil indicates the presence of 42 per cent. methyl cinnamate.

Oil of Gastrochilus Pandurata Ridl.—(N. O. Zingiberaceæ). This oil was almost colorless; its odor strongly resembled those of estragon and basilicum oils. d_{15° 0,8746; α_D + 10° 24′; $n_{D_{20^\circ}}$ 1,48957; acid no. 0; ester no. 17,3; imperfectly soluble in 10 vols. 80 per cent. alcohol, but making a clear mixture with 90 per cent. alcohol.

PHILADELPHIA COLLEGE OF PHARMACY—SEMI-ANNUAL MEETING.

The semi-annual meeting of the College was held September 25th, at 4 P.M., in the Library, the President, Howard B. French, presiding. Eighteen members were present. The minutes of the quarterly meeting held June 26th were read and approved. The minutes of the Board of Trustees for the meeting held June 6th were read by the Registrar, and approved.

The Committee appointed to draft suitable resolutions to the memory of Wallace Procter, reported by its Chairman, Professor

Joseph P. Remington, the following memorial, which was on motion adopted, and an engrossed copy directed to be sent to Mrs. Procter.

"WALLACE PROCTER.

The Philadelphia College of Pharmacy mourns the loss of one of her faithful sons, who as student, graduate, alumnus, member of the College, Board of Trustees, or Chairman of the Committee on Examinations, served the College faithfully for forty-two years. He departed this life May 27, 1911. No service was too arduous for him when he felt he could aid his Alma Mater. Skilled in the art and science of his profession he brought his talents to bear in the direction which seemed to him to be productive of good results to the institution. The Philadelphia College of Pharmacy places on record its highest sense of appreciation of the loving services of Wallace Procter."

The Committee on Nominations presented list of nominees for Trustees.

A communication was read from Mr. R. W. Cuthbert requesting his name be withdrawn from the list of nominees for Trustees.

The delegates to the American Pharmaceutical Association to the meeting held in Boston, August 14–18, reported verbally through Professor C. B. Lowe. A number of items of interest were related in addition to the extended report of the meeting published in the AMERICAN JOURNAL OF PHARMACY, page 436, in the September number.

Amendment to By-laws: The amendment to Article XI, Section I, of the By-laws of the College, laid over from the previous meeting, was taken up, and on motion adopted. The amended section reads as follows: The pharmaceutical meetings of the College shall be held for the purpose of discussing scientific questions and subjects relating to trade interests once in every month, from October until May, both inclusive, at such times as the Committee on Pharmaceutical Meetings may determine. This amendment will enable the Committee to name a time that will enable a larger number of the members and students to be present.

The President appointed the following as the Committee on Membership: Charles H. LaWall, Chairman; E. M. Boring, Richard H. Lackey, Richard M. Shoemaker, C. A. Weidemann.

Election of Honorary Members: The names of those proposed for Honorary Members at the June meeting, and laid over for action till the September meeting, were then read. Mr. J. W. England was appointed teller, who, after a ballot was taken, reported the unani-

mous election of Professor Oscar Oldberg, who retires as Dean of the School of Pharmacy of the Northwestern University of Illinois, after having completed twenty-five years of service in educational work and to the general uplift of pharmacy, and of Professor Edgar F. Smith, Professor of Chemistry at the University of Pennsylvania and now Provost of that institution, distinguished for his studies in electro-chemistry and author of very many scientific and educational papers.

The President announced the death of Dr. George R. Vernon, on September 16, 1911, a graduate of the class of 1871 and a member of the College since 1872.

Election of Trustees: The list of nominees was read. C. Stanley French and Mitchell Bernstein were appointed tellers, who, after a ballot was taken, reported the election of George M. Beringer, Joseph W. England and C. Mahlon Kline, whereupon the President declared them elected to the Board of Trustees for the ensuing three years.

C. A. Weidemann, M.D.,
Recording Secretary.

ABSTRACTS FROM THE MINUTES OF THE BOARD OF TRUSTEES

June 6—Sixteen members were present. Committee on Property—reported estimates for repairing and also replacing the water tank on the roof of the building, and stated that the tank builders thought the condition of the present tank was such that it would be much better to replace it than to make repairs; and the Committee further suggested the advisability of increasing the capacity to 8000 gallons provided the supports would admit of it. The Committee was empowered to proceed with the work as in their judgment was best.

The Committee on Library reported the receipt of the first installment of the Encyclopedia Brittanica. Several books had been donated by Professor Remington. Ninety-four books were accessioned, classified and shelf-listed, making a total of seventeen hundred and fifty-seven books ready for the shelves. Seventy-five persons consulted the Library during May.

The Committee on Examinations referred to the form now used for special certificates, objection was had to the present form as it looked so much like a Diploma. After discussion a Committee

consisting of Howard B. French, W. L. Cliffe and Professor Joseph P. Remington was appointed to consider the matter.

The Committee on Commencement reported all the exercises attending Commencement had passed off nicely, and it was moved that a resolution of thanks be tendered the Speaker and Minister officiating. So ordered. The Committee reported that the Commencement in 1912 would take place on Thursday, May 23rd, at the Academy of Music, which would be engaged for the occasion.

The Treasurer was authorized to pay the salary lists during the summer of the Board, and such other bills as were approved by the Committee on Accounts and Audits.

(Signed) C. A. WEIDEMANN,
Secretary.

PHARMACEUTICAL MEETINGS.

The pharmaceutical meetings of the Philadelphia College of Pharmacy have been held for many years on the third Tuesday of the month from October to May. The section in the article of the by-laws of the college, relating to the date of these meetings, has been changed (see account of the September meeting of the college given elsewhere in this issue), leaving it optional with the committee to fix the date of each meeting. The first meeting was held on Monday, October 16th, at 3 P.M., Mr. William L. Cliffe acting as chairman.

Mr. George M. Beringer presented a communication upon "The Pharmacists' Plea for a Rational Pharmacopœia" and Mr. Otto Raubenheimer, of Brooklyn, spoke upon "The List of Proposed Deletions" of the new U. S. Pharmacopœia. Both speakers referred to a number of substances which they considered should be included in the new Pharmacopœia as in some cases the preparations of the drugs were retained. Professor Remington, chairman of the Committee of Revision of the U. S. Pharmacopœia, stated that in some instances the omissions were due to mere oversight and that nearly all of the substances referred to were being further considered either with regard to their inclusion or deletion in the forthcoming Pharmacopœia. He also emphasized the importance of abiding by the majority vote as it is impracticable to do otherwise.

The discussion was also participated in by Dr. Lowe, Mr. H.

P. Busch, Dr. H. C. Wood, Jr., and Professor Kraemer. Dr. Lowe referred to a few of the drugs which are to be retained and which he thought were too seldom used to merit a place in the pharmacopœia. Mr. Busch said that the pharmacopœia is no longer a theoretical standard but should be a book of practical standards for commercial use. Dr. Wood especially called attention to the large amount of work which had been done by the Sub-committee on Scope of the Pharmacopœia in arriving at its conclusions as presented in the tentative report already published. Professor Kraemer emphasized the desirability of deleting obsolete substances and their preparations and said that the work in connection with the deletions and additions of the pharmacopœia is of necessity a compromise and that the work thus far in his opinion had been well done.

President French sent several interesting specimens for the museum. Among these were some Chinese tung nuts from which China oil is made; specimens of China wood oil and soya bean oil; and four large photographs showing Chinese coolies handling "wood oil" in Hankow, China. The specimens and photographs were given President French by L. C. Gillespie & Sons, whose office is located in Hankow, China. Mr. French also sent a bottle of camphorated spirits which was made and put up by A. S. Watson & Co., Hong Kong, China. Prof. Charles H. LaWall made a polariscopic examination of the specimen and found it to contain 10 per cent., or a normal amount of camphor, for this preparation, and the identity tests showed that the camphor is of natural and not of synthetic derivation.

Professor Samuel P. Sadtler presented a specimen of mangrove bark which assayed 46.05 per cent. of tannin.

Messrs. Parke Davis & Co. presented to the college a large photograph in colors of medicinal plank, the drugs derived from which are standardized by chemical or physiological means. They also sent for distribution to the members present, a booklet giving valuable information on those drugs which are standardized by chemical or physiological means and also illustrated with handsome photographs in colors of the plants from which they are derived.

Professor Kraemer exhibited a large gourd containing Barbadoes aloes which he had recently purchased for the college. He stated that from the information that he had thus far received the aloes industry had been resumed in Barbadoes during the past few years and that the annual crop is said to be about 1500 pounds.

H. K.

NEW YORK GERMAN APOTHECARIES' SOCIETY.

The New Yorker Deutscher-Apotheker-Verein, the oldest pharmaceutical association in the United States, celebrated the sixtieth anniversary of that society on September 28th with a great Kommers in the banquet hall of Terrace Garden, New York City. It is now sixty years since Messrs. Ramsperger, Waldorf, Gnadendorf, Hasse and Rudolfi came together in Zocke's restaurant and determined to meet regularly and to enjoy the German "Gemütlichkeit" for which each one was yearning. They elected Mr. Gustav Ramsperger the first President, and it was indeed a thrilling occasion to have him as the sole survivor of the old guard, present to recite the history of this organization from the time of its humble beginnings, until to-day it is one of the strongest and most influential organizations in America.

These pioneers of the early organization met together late at night, after their stores were closed, not only to think of the Fatherland and the ties across the sea, but to become the most intense and virile of Americans. During these hours of relaxation and enjoyment they were thinking of the advancement of their business and profession. Each one possessed a vigorous intellect and was dominated by a high ethical standard. And as they drank from their steins of beer and smoked their cigars, they discoursed on "the doings of the day," the humorous incidents in the store, and the difficulties of the prescription counter. They furthermore read original poems and sang original songs. Some of them under the chairmanship of Mr. Weissmann started a pharmaceutical museum. Here were gathered together the galenical preparations obtained from different apothecaries and which demonstrated the necessity for uniformity of processes. In fact, it was this work which suggested the National Formulary. In the early days there were but twenty-two members and as they came to know each other better, the ties became so strong and the loyalty to the Verein so great that the association must be perpetuated and they enrolled members of German descent, until to-day there are several hundred members.

Dr. William C. Alpers, one of the best known and most esteemed of American pharmacists, acted as toastmaster. He was overflowing with enthusiasm and good humor and conducted the Kommers in the true spirit of the Verein. Mr. Carl F. Schleussner, an ex-president of the Verein, presented to Mr. Ramsperger a loving-cup on the

occasion. The anniversary was marked by the presence of Dr. Abraham Jacobi, president of the American Medical Association, Prof. Joseph P. Remington and Prof. John Uri Lloyd, all three of whom were made honorary members. The address of Dr. Alpers, upon giving the diplomas to Prof. Remington and Prof. Lloyd, echoes so much of the sentiment of the society that it is here given in its entirety. It is as follows:

"The pleasing and cheerful words that you have just addressed to us have gone to our hearts, and come back from there like a joyous and responsive echo. It is not often that we have Americans prominent in pharmacy as you two, among us. Our society is a German one, and the official language here is the German tongue. We watch over German features and are proud of them not because we dislike the English language, nor because we think less of things American. Our daily surroundings, our aspirations, our hopes in business, as in social matters, in fact, all our daily activities are American, and we are Americans in every sense of the word. Indeed, no one may become a member of this society unless he is a citizen of the United States.

"If yet we cling to German customs, we do so because our meetings are a refuge from our daily toil. Here we come back to the days of our youth, here we find that recreation that is needful to us, here we once more revel in those ideals which fill so completely the heart of the German youth: and we believe this change in language, this change in thought, this return to days long past, and never to be recalled, gives us strength and encouragement, and in the enjoyment of German 'Gemütlichkeit' we find ample recompense for our daily duties. And more than this, the intercourse between German and American civilization has increased from day to day during the last few decades.

"We have prized it here for sixty years and we are proud that the spirit that has kept this society alive and made it grand and given it influence and importance, has added greatly in bringing together the scientific bodies of the two great nations. To us Germans, our new country is our bride, for whose life and honor we are ready to sacrifice all we have, but in our loyalty and affection for her we will never forget our loving mother across the sea, and always have ready for her a resting place at our hearth.

"It is in this feeling of pleasure and pride that we welcome you to-night in our midst, you whom we believe to be the two most typi-

cal representatives of American pharmacy. You both have risen from the low position as apprentice in a drug store to high places in our profession. You, Joseph P. Remington, as chairman of the Committee of the Revision of the Pharmacopœia, have attained what I consider the highest honor that American pharmacy can confer. And you, John Uri Lloyd, have gained an international reputation as scientist and author, and in commercial pursuits have not forgotten the sweeter and gentler side of human nature, and depicted them in a masterful way in your beautiful novels.

"It is therefore in this spirit of pride and friendship, which goes out from us to you, that we have decided to confer upon you both the honorary membership of the German Apothecary Society. We want to emphasize herewith our loyalty for American pharmacy and our admiration for American science. We want to have it understood that we are American in heart and soul, and further, we want to give expression to our personal admiration and love with which our hearts go forth to you as the best men that American pharmacy has produced. And finally, speaking in a broader sense, we wish to accentuate the bonds of friendship that exist among scientific men of the two nations, Germany and the United States, that broad and noble friendship which alone makes for higher civilization, for better knowledge, for better understanding of all that is grand and ennobling in either country and that brings the two great nations closer and closer together in a common purpose. It is in this spirit that I hand you these diplomas, and I know that you will accept them in the same way."

Addresses were also made by Mr. Felix Hirseman, an ex-president of the Verein, who reviewed the history of pharmacy in New York during the past 60 years; Mr. Carl Hauser, the well-known humorist, had for his theme, "Sixty Years as the Customer of the Apothecary." The newly-elected honorary members also were called upon to respond.

The programme was gotten up in pamphlet form, containing songs written for the occasion and excellent caricatures of some of the members and guests. The officers of the New Yorker Deutscher-Apotheker-Verein at present are: president, George Klinan; honorary president, Gustav Ramsperger; vice-presidents, Dr. C. F. Klippert and Paul F. Gebicke; permanent secretary, Otto P. Gilbert; corresponding secretary, E. A. Boetzel; treasurer, Robert S. Lehman; recorder, George Leinecker; librarian, George C. P. Stolzen-

burg; board of directors, E. C. Goetting, C. F. Schleussner and Felix Hirseman. Otto P. Gilbert was chairman of the Jubilee Committee, which deserves much credit for the excellent programme and menu, the selection of speakers and the entertainment provided.

H. K.

UNIVERSITY OF THE PHILIPPINES.

Course in Pharmacy.

The Board of Regents of the University of the Philippines, on January 12, 1911, decided to establish a course in pharmacy, in the College of Liberal Arts. Students will be admitted to the first year of the course at the opening of the school year 1911–1912.

The course in pharmacy will require three full years of study, and will lead to the degree of Graduate in Pharmacy. A fourth year will be offered leading to the degree of Pharmaceutical Chemist.

The entrance requirements for the course in pharmacy are those for entrance to the College of Liberal Arts.

No students will at present be admitted to the course in pharmacy with advanced standing; nor will any work of the course beyond the first year be given during the school year 1911–1912.

The second year of the course in pharmacy will be opened in 1912; the third year in 1913.

Students will register for the course in pharmacy with the dean of the College of Liberal Arts.

CORRESPONDENCE.

Physiological Methods for the Standardization of Digitalis.

Editor of the American Journal of Pharmacy,
Philadelphia, Pa.

Dear Sir:

In a paper of mine which you were good enough to publish ("Physiological Methods for the Standardization of Digitalis," Am. Jour. of Pharm., May, 1911) I made the statement that Dr. Houghton advocated the use of ouabain as a standard preparation in testing the members of the digitalis group on frogs. I have since learned that Dr. Houghton employs crystalline Kombé strophanthin, believing it superior to the Gratus strophanthin. If you would be so kind as to publish this correction, I should be very much obliged.

Very truly yours,

May 26, 1911. Chas. C. Haskell.

National Formulary.

To the Editors of Pharmaceutical Journals and the Secretaries of Local Branches of the American Pharmaceutical Association:

I am sending you herewith, for general discussion, an installment of formulas that it is proposed to add to the National Formulary, and trust that you will be willing to bring them to the attention of members of the American Pharmaceutical Association and other pharmacists and druggists who may be interested.

The object of giving publicity to proposed changes and additions is to elicit, if possible, comment and criticism before the final publication of the Fourth Edition of the National Formulary so as to avoid, as much as possible, untoward criticism of the book after its promulgation as a national standard.

If editors of pharmaceutical journals will give publicity to the material as offered and if secretaries of local branches of the American Pharmaceutical Association will offer this material for experimentation and discussion there will be no danger of incorporating into the forthcoming edition of the National Formulary formulas that have not been thoroughly tried in the different sections of the country under varying conditions.

In this connection it should be remembered that failure to criticize any or all of these formulas must be taken as a tacit acquiescence and will necessarily lead members of the Committee on National Formulary to infer that the formulas as offered are acceptable.

Trusting that you will be willing to co-operate in the work of perfecting the National Formulary, I am

Fraternally yours,

M. I. Wilbert.

The following are some of the new formulas that have been suggested for inclusion in the forthcoming edition of the National Formulary. The committee is desirous of having them thoroughly tried by pharmacists in different sections of the country so as to avoid, as much as possible, unfavorable comment after the final publication of the book. Comments and criticisms, based on practical experiences, will be welcome. All communications should be

addressed to the Chairman of the Committee, Prof. C. Lewis Diehl, 932 Cherokee Road, Louisville, Ky., who will submit the comments to the sub-committee having the matter in charge.

Elixir Amygdalæ Compositum.

(Compound Elixir of Almond.)

Oil of bitter almond	0.5 c.c.
Vanillin	1.0 Gm.
Stronger orange flower water	150.0 c.c.
Alcohol	50.0 c.c.
Syrup	400.0 c.c.
Kieselguhr	10.0 Gm.
Distilled water, a sufficient quantity to make	1000.0 c.c.

Dissolve the oil of bitter almond and the vanillin in the alcohol, add the syrup, and then the stronger orange flower water, then the distilled water in several portions, shaking the mixture thoroughly after each addition; then add the kieselguhr, mix and filter, returning the first portion of the filtrate, if necessary, until it runs through clear. Lastly, wash the filter with sufficient of a mixture of alcohol 1 volume and distilled water 19 volumes, until 1000 c.c. of product is obtained.

Elixir Glycyrrhizæ Aquosum.

(Aqueous Elixir of Glycyrrhiza. Aqueous Elixir of Licorice.)

Fluidextract of glycyrrhiza	150 c.c.
Compound spirit of cardamom	5 c.c.
Stronger orange flower water	200 c.c.
Glycerin	150 c.c.
Syrup	150 c.c.
Water, a sufficient quantity to make	1000 c.c.

Mix and filter.

Elixir Rubrum.

(Red Elixir.)

Cudbear	2 Gm.
Aromatic elixir	1000 c.c.

Add the cudbear to the aromatic elixir, in a suitable container, and allow the mixture to stand for six hours with occasional agitation, then filter.

Elixir Trium Bromidorum.

(Elixir of Three Bromides.)

Ammonium bromide	80 Gm.
Potassium bromide	80 Gm.
Sodium bromide	80 Gm.
Cudbear	2 Gm.
Compound elixir of almond, a sufficient quantity to make	1000 c.c.

Dissolve the bromides in sufficient compound elixir of almond, add the cudbear and allow the mixture to macerate in a closely stoppered bottle for six hours, with occasional shaking. Finally filter.

Elixir Formatum.

(Elixir of Formates.)

Potassium formate	50 Gm.
Sodium formate	50 Gm.
Aromatic elixir, a sufficient quantity to make	1000 c.c.

Dissolve the formates in the aromatic elixir and filter.

Elixir Formatum Compositum.

(Compound Elixir of Formates.)

Monohydrated sodium carbonate	23 Gm.
Magnesium carbonate	20 Gm.
Strontium carbonate	25 Gm.
Lithium carbonate	8 Gm.
Quinine alkaloid	7.7 Gm.
Formic acid	200 c.c.
Compound spirit of cardamom	10 c.c.
Acetic ether	2 c.c.
Alcohol	100 c.c.
Glycerin	300 c.c.
Purified talc	20 Gm.
Distilled water, a sufficient quantity to make	1000 c.c.

Add the formic acid to 300 c.c. of distilled water and in this dissolve the carbonates, and then add the quinine; to this solution add the glycerin and then the alcohol, previously mixed with the compound spirit of cardamom and the acetic ether, agitate thoroughly, and add sufficient distilled water to make the product measure 1000 c.c. Then add the purified talc, mix and filter with sufficient mixture of alcohol 1 volume, distilled water 9 volumes, until 1000 c.c. of finished preparation is obtained.

ELIXIR CARDAMOMI COMPOSITUM.

(Compound Elixir of Cardamom.)

Compound spirit of cardamom	10 c.c.
Alcohol	90 c.c.
Syrup	400 c.c.
Kieselguhr	10 Gm.
Distilled water, a sufficient quantity to make	1000 c.c.

Mix the compound spirit of cardamom with the alcohol, add the syrup, and then the distilled water in several portions, shaking the mixture thoroughly after each addition; then add the kieselguhr, mix and filter, returning the first portion of the filtrate, if necessary, till it runs through clear. Lastly, wash the filter with sufficient of a mixture of alcohol 1 volume and distilled water 9 volumes, until 1000 c.c. of product is obtained.

SPIRITUS CARDAMOMI COMPOSITUS.

(Compound Spirit of Cardamom.)

Oil of cardamom	20.0 c.c.
Oil of orange	20.0 c.c.
Oil of cassia	2.0 c.c.
Oil of cloves	1.0 c.c.
Anethol	1.0 c.c.
Oil of caraway	0.1 c.c.
Alcohol, a sufficient quantity to make	200 c.c.

Mix the oils with 140 c.c. of alcohol, finally adding a sufficient quantity of alcohol to make the spirit measure 200 c.c.

ELIXIR VANILLINI COMPOSITUM.

(Compound Elixir of Vanillin.)

Compound spirit of vanillin	20 c.c.
Alcohol	80 c.c.
Glycerin	25 c.c.
Syrup	300 c.c.
Kisselguhr	10 Gm.
Tincture of caramel	20 c.c.
Distilled water, a sufficient quantity to make	1000 c.c.

Mix the compound spirit of vanillin with the alcohol, add the glycerin, and then syrup and distilled water in several portions, shaking the mixture thoroughly after each addition; then add the kieselguhr, mix and filter, returning the first portion of the filtrate, if necessary, till it runs through clear. Lastly, wash the filter with a mixture of alcohol 1 volume and distilled water 9 volumes, until 980 c.c. of product is obtained. Finally, add 20 c.c. of tincture of caramel.

SPIRITUS VANILLINI COMPOSITUS.

(Compound Spirit of Vanillin.)

Vanillin	40 Gm.
Oil of orange	10 c.c.
Oil of cardamom	2 c.c.
Oil of cassia	1 c.c.
Alcohol, a sufficient quantity to make	200 c.c.

Dissolve the vanillin and the essential oils in 150 c.c. of alcohol and then add sufficient alcohol to obtain 200 c.c. of product. Store in tightly stoppered amber-colored vials, in a cool place, protected from light.

ELIXIR AURANTII AMARI.

(Elixir of Bitter Orange. Elixir of Curacao.)

Oil of bitter orange	4 c.c.
Tincture of bitter orange peel	20 c.c.
Alcohol	300 c.c.
Stronger orange flower water	20 c.c.
Syrup	400 c.c.
Kieselguhr	10 Gm.
Distilled water, a sufficient quantity to make	1000 c.c.

Mix the oil of bitter orange and the tincture of bitter orange peel with the alcohol, add the syrup, and then the stronger orange flower water, and then the distilled water, in several portions, shaking the mixture thoroughly after each addition; then add the kieselguhr, mix and filter, returning the first portion of the filtrate, if necessary, till it comes through clear. Lastly, wash the filter with sufficient of a mixture of alcohol 3 volumes and distilled water 7 volumes, until 1000 c.c. of product is obtained.

ELIXIR SODII SALICYLATES COMPOSITUM.

(Compound Elixir of Sodium Salicylate.)

Sodium salicylate	80 Gm.
Fluidextract of cimicifuga	32 c.c.
Fluidextract of gelsemium	16 c.c.
Potassium iodide	16 Gm.
Purified talc	15 Gm.
Aromatic elixir, a sufficient quantity to make	1000 c.c.

Dissolve the sodium salicylate and potassium iodide in 800 c.c. of aromatic elixir, add the fluidextracts and then sufficient aromatic elixir to make 1000 c.c. Add the purified talc, mix and filter.

Compound elixir of sodium salicylate should be kept in amber-colored bottles, protected from the light.

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COLORIMETRIC AND PHYSIOLOGICAL ESTIMATION OF THE ACTIVE PRINCIPLE OF THE SUPRARENAL GLAND.

By Worth Hale and Atherton Seidell.

[Hygienic Laboratory, U. S. Public Health and Marine-Hospital Service, Washington, D. C.]

Of the many color tests which have been proposed for the active principle of the suprarenal gland, none appears to have been developed to the accuracy required of a quantitative method. Several have been used for comparative studies on glands from different sources, but, so far as shown by the literature, no attempts have been made to correlate the results obtained by color tests with the activity as determined by physiological methods.

In applying a number of the better known color reactions to a series of desiccated suprarenal glands, for the purpose of selecting a suitable one for the forthcoming revision of the U. S. Pharmacopœia, it was noticed that considerable variation in the intensities of the colors from the several samples was obtained; preliminary blood pressure experiments with some of these samples confirmed the differences indicated by the color tests. It thereupon appeared probable that a colorimetric method which would yield results in close agreement with those obtained by the physiological standardization, could be developed.

Experiments with the various color tests which have been proposed, indicated that the potassium permanganate, the potassium ferricyanide with dilute ammonia, the sodium hydroxide, and the potassium permanganate with lactic acid, reagents, gave little promise of success. The iodine method of Abelous, Soule and

Toujan,[1] the mercuric chloride test of Comessati,[2] and the iodic acid reaction of Krauss[3] and independently described by Fränkel and Allers,[4] were found to be much more delicate. The suggestion of Abel[5] that the fleeting green color produced by ferric chloride could be rendered more permanent by addition of an excess of potassium benzene thiosulphonate was not followed up since the ferric chloride test is of such general applicability that it was thought to be less characteristic of the epinephrine base than the three tests mentioned above.

According to the iodine test of Abelous, Soule and Toujan, 10 c.c. of the 1 : 10,000 epinephrine solution is mixed with 5 c.c. of 0.1 n iodine and allowed to stand 15 minutes, the excess of iodine is then discharged with 0.1 n thiosulphate, the solution diluted to 50 c.c. and its color compared with standards made in the same way with a solution of the pure base. Experiments showed, however, that the intensity of the pink color increased with length of time allowed before the discharge of excess of iodine; moreover, the tints varied to such an extent that accurate comparison did not appear possible, and all the colors faded fairly rapidly on standing. With the mercuric chloride test which consists in adding a few drops of saturated $HgCl_2$ to the epinephrine solution and heating to the boiling point, the colors developed rather slowly, and furthermore, variations in shade and intensity were obtained from equal amounts of the active principle. The most satisfactory results were obtained with the iodic acid test, viz., by heating just to boiling, the mixture of equal parts of the solution to be tested and 0.2 per cent. KIO_3 solution. The addition of a few drops of dilute phosphoric acid as prescribed by Fränkel and Allers was found to be a disadvantage since it caused much more rapid fading of the color. Using a standard epinephrine solution containing 1 part per 50,000 of the pure base dissolved with the aid of twice the calculated amount of HCl to yield the hydrochloride, the pink color was found to remain practically unchanged for several days.

Although the color produced as above mentioned is fairly stable and would undoubtedly serve as a standard with which to compare

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[1] *Compt. rend. soc. biol.*, **58**, 301, 1905.
[2] *Arch. Exp. Path. u. Pharm.*, **62**, 190, 1909–10.
[3] *Apoth. Ztg.*, **23**, 70, 1908.
[4] *Biochem. Ztschr.*, **18**, 40, 1909.
[5] *Johns Hopkins Hosp. Bull.*, **12**, 342, 1901.

unknown samples, it was considered desirable to have color standards which were certain to remain unchanged for an indefinite period. A casual examination of the pink tint produced from the epinephrine base by boiling with potassium iodate solution showed it to consist of a mixture of red and yellow. Unsuccessful efforts were made to find a particular dye which would yield an aqueous solution corresponding exactly to the tint in hand; mixtures of dyes would probably serve, but a better source was found in the color standards adopted by the committee on Standard Methods of Water Analysis of the American Public Health Association,[6] viz.: (a) platinum solution made by dissolving 20 gms. K_2PtCl_6 in a small amount of distilled water, adding 100 c.c. of conc. HCl, and diluting to 1000 c.c., (b) Cobalt solution made by dissolving 12 gms. of $CoCl_2$ $6H_2O$ in distilled water, adding 100 c.c. of conc. HCl, and diluting to 1000 c.c. By mixing these two solutions in approximately the proportion of 1 of the former to 3 of the latter the tint is almost indistinguishable from that produced from the epinephrine. The intensity of this color standard can then be adjusted by dilution to correspond exactly with that obtained by mixing 5 c.c. of the 1:50,000 solution of the ash free active principle of the suprarenal (dissolved with the aid of twice the calculated amount of HCl), with 5 c.c. of a 0.2 per cent. KIO_3 solution, thus yielding 0.1 mg. active principle per 10 c.c., heating just to the boiling point and after 15 minutes comparing with the permanent color standards in a suitable colorimeter. After standardization, a series of test tubes may be prepared with dilutions of the permanent standard corresponding to 0.01, 0.02, 0.03, 0.04, 0.06, 0.08 and 0.10 mg. active principle per 10 c.c. and the test tubes then labelled and sealed.

Various experiments made by boiling given amounts of the desiccated suprarenal glands with water, dilute HCl and mixtures of these with 0.2 per cent. KIO_3 solution indicated that the principal difficulty in the colorimetric determination is caused by the yellowish extractive material present in the aqueous solution of the sample. This in many cases interferes with the accurate estimation of the intensity of the pink color, and therefore leads to low results. It was found that the inconvenience due to yellowish tint was greatest when a larger amount of sample was used and the

[6] *Jour. Infectious Diseases,* Supplement I, p. 34, May, 1905.

resulting solution diluted to the required strength than when a proportionately smaller amount of sample was used and the solution not diluted.

With samples containing from 0.2 to 0.8 per cent. of the active principle, 0.01 gm. is placed in a test tube with 5 c.c. of dilute HCl (2.5 c.c. 0.1 n HCl per 100 c.c.) and 5 c.c. of 0.2 per cent. KIO_3 solution, the mixture heated just to the boiling point and allowed to stand 15 minutes; it is then filtered and the color compared with the series of standards corresponding to 0.01 to 0.10 mg. per 10 c.c. The position of the unknown can in practically all cases be fixed in this series with reasonable certainty.

Determinations were made as above described upon nine samples of commercial desiccated suprarenals obtained from two firms and one sample of 1 : 1,000 solution of the active principle which had been in the laboratory some time. The results were as follows:

TABLE I.

Sample No.	Per cent. active principle.
362	0.6
363	0.6
364	0.6
365	0.8
366	0.2
367	0.8
368	0.4
369	0.4
370	less than 0.03
1 : 1,000 solution	0.03.

THE PHYSIOLOGICAL EXPERIMENTS.

In the quantitative physiological assay of epinephrine a number of different methods have been proposed, all being based on some physiological action of the base. Of these the one most commonly employed is that of determining the relative rise in blood pressure as compared with a given amount of the pure base; and a careful analysis of the other methods, the frog's eye test, the use of arterial strips and the minimum lethal dose,[7] indicates that with proper precautions this is also the most satisfactory and accurate. Of the several animals upon which blood pressure experiments might be carried out dogs appear to give the best results. For the purpose

[7] Schultz: Bull. 55, Hyg. Lab., U. S. P. H., and M. H. S., 1909.

of these tests full grown dogs of small size, 5 to 10 kilograms body weight, were chosen. They were anæsthetized by the injection of 0.015 gm. morphine sulphate per kilo, and sufficient ether given to insure complete anæsthesia during the operative procedure. The ether was then withdrawn although, if the animal showed signs of returning consciousness, especially as noted by irregularities in the blood pressure curve, it was again administered in small quantities during the course of the experiment. A cannula was introduced into the carotid and connected with a mercury manometer to secure a blood pressure tracing. Cannulæ were also introduced at the same level into both the right and left femoral veins for the injection of the drug to be tested. Both vagi were cut and artificial respiration maintained throughout the experiment.

To prepare the desiccated suprarenal extract for injection 50 milligrams were added to 40 c.c. Ringer solution and acidulated by the addition of 3 drops of 10 per cent. HCl. This was then slowly brought to a boiling temperature and allowed to cool for ten minutes, whereupon the solution was passed through a filter and the residue washed with a sufficient amount of warm Ringer solution to bring the total up to 50 c.c., thus making 1 c.c. of the solution represent 1 milligram of the desiccated gland. This procedure, however, was altered in the case of two samples, Nos. 366 and 370, owing to their relative inactivity. These samples were each made up so that 1 c.c. of the resulting solution equalled 5 milligrams of the gland, thus securing a suitable rise in pressure without using too large doses for intravenous injection.

The rise in pressure from equal doses of the same preparation varies in different animals and in the same animal from time to time during the experiment. This is probably due in large measure to a varying depth of anæsthesia and to varying sensitiveness of the vasomotor centre and the musculature of the arterioles. At any rate it becomes necessary in quantitative work to inject, alternately with the sample which is being assayed, a definite amount of the purified base, continuing in this until rises of equal height are obtained. As duplicate determinations there should then be injected ratios of the amount necessary to produce the same result and these larger or smaller amounts of the known and the unknown solution should likewise produce equal rises in pressure. Many of the necessary details of this method have been discussed by Dr. Schultz in Hygienic Laboratory Bulletins Nos. 55 and 61.

The solution of the purified base used in these experiments either was made up fresh every day or it was made up by diluting a stock 1 to 10,000 solution which was kept on ice to prevent deterioration. Dilutions of 1 to 50,000 and 1 to 100,000 were used and the injection of both the known and unknown solutions varied from 0.5 to 1.0 c.c.

The injections might possibly all be made through one cannula, but to obviate the necessity of washing out the residual solution each time, cannulæ are placed in the right and left femoral vein, one for injecting the known and the other the unknown solution. As injections made at different rates produce different results it is necessary to make both injections at as nearly the same rate and as rapidly as possible.

Two tables are given to show the method of arriving at the assay value of a given product.

TABLE II.

Sample desiccated suprarenal glands, No. 363, dog 7.6 kg. body weight; morphine sulphate 0.015 gm. per kg. subcutaneously. Both vagi cut. Epinephrine base in 1 to 100,000 acidulated Ringer solution. No. 363 suprarenal gland 1 mg. to 1 c.c. acidulated Ringer solution.

Time.	Preparation.	Dose.	Blood pressure before.	Blood pressure after.	Rise in millimeters.
11.48	Epinephrine	0.5 c.c.	166	206	40
11.51	363	0.5 mg,	164	204	40
11.56	363	0.5 "	162	200	38
12.02	Epinephrine	0.4 c.c.	156	192	36
12.05	363	0.4 mg.	156	192	36
12.12	Curare				
12.17	Epinephrine	0.6 c.c.	152	188	36
12.19	363	0.6 mg.	148	182	34
12.23	363	1.0 "	144	190	46
12.26	Epinephrine	1.0 c.c	138	182	44
12.29	363	1.0 mg.	140	186	46

It is easily seen from the above record that 1 milligram of the desiccated gland gave the same rise as 1 c.c. of a 1 to 100,000 epinephrine solution, or 0.01 milligram estimated as the base. The desiccated gland therefore contained 1 per cent. of the base.

Table III further illustrates the method of arriving at the assay value.

TABLE III.

Legend the same as for Table II. Sample No. 368 was used, 1 milligram to 1 c.c.; Epinephrine solution 1 to 100,000 solution.

Time.	Preparation.	Dose.	Blood pressure before.	Blood pressure after.	Rise in millimeters.
1.30	Epinephrine	0.6 c.c.	128	154	26
1.33	368	0.6 mg.	128	150	22
1.38	Epinephrine	0.6 cc.	126	154	28
1.40	368	0.7 mg.	124	150	26
1.43	Epinephrine	0.5 c.c.	124	150	26
1.49	"	0.75 c.c.	132	164	32
1.52	368	1.0 mg.	122	150	28
1.54	368	1.0 "	120	148	28
1.57	Epinephrine	0.7 c.c.	122	152	30
2.01	368	0.8 mg.	126	146	20

From this table it will be noted that the ratios of 0.5 of the known to 0.7 of the desiccated gland solution and 0.7 to 1.0, respectively, gave like rises in temperature. One milligram of the desiccated drug therefore contained the amount of epinephrine base in 0.7 c.c. of the known solution, 0.007 or 0.7 per cent.

These two tables are from one of the final experiments after the approximate values of the unknown had been worked out.

Below is given a table showing the results obtained from the various samples by the physiological and the colorimetric method of assay.

TABLE IV.

Sample No.	Per cent Active Principle by Colorimetric Method	Per cent Active Principle by Physiological Method
362	0.6	1.0
363	0.6	1.2, 1.0, 1.0
364	0.6	1.0
365	0.8	1.1, 1.1
366	0.2	0.3, 0.2
367	0.8	1.1, 1.0, 1.1
368	0.4	0.7
369	0.4	0.7
370	less than 0.03	0.04
1 : 1000 solution	0.03	0.035

From this table it will be seen that fairly large differences exist in the two sets of values; however, it will be noted that a close parallelism exists between them. The results by the physiological

method being some 30 per cent. higher in most cases. We are unable at present to account for this, especially since the same sample of the pure ash free active principle was used as the basis for the determinations by the two methods. Apparently the most plausible explanation is that referred to above, namely, that the yellowish extractive material yielded by the samples is the cause of the lower readings by the colorimetric method. In spite of these variations, however, we believe that this test is by far the most satisfactory one at present available and furnishes a means for closely estimating the relative value of different lots of desiccated suprarenal glands and 1 : 1000 solutions of the active principle. We hope to be able in the near future to extend our experiments to many other samples, both of the desiccated glands and the commercial 1 to 1000 solutions and trust that we will be able to remedy the cause of the present differences in values obtained by the two methods.

In conclusion special attention should be called to the very wide differences in activity found for the various commercial samples of desiccated glands and the considerable diminution in strength of a 1 : 1000 solution of the active principle. Such wide variations have so far not been reported for the commercial glands and were not expected when we undertook these experiments. They illustrate very forcibly the need of just such a simple method of control of this product as is described in the present paper.

ON THE PHARMACOPŒIAL ASSAY OF CITRAL IN LEMON OIL.

By J. R. Rippetoe, P.D., and Louis E. Wise, Ph.D.

The determination of Citral has for several years past been the subject of considerable investigation. In 1906 Chace [1] proposed a rapid method for the estimation of this aldehyde, which is applicable to the analysis of lemon oils and extracts and which time has shown to be admirably suited to the needs and requirements of the importer of the essential oils. Somewhat more recently Bennet,[2] modifying a method of Walther,[3] has suggested a means of analysis

[1] *Journal of the American Chemical Society,* **28,** 1472.
[2] *Analyst,* **34,** 1417.
[3] *Pharm. Centr.,* **40,** 621.

depending on the use of hydroxylamine hydrochloride, and Romeo [4] outlined a titration method which was published by the Messina Chamber of Commerce and successfully followed in the analysis of a number of pure oils.

In 1909 Hiltner [5] published the description of a colorimetric method which together with that of Chace [1] has been outlined by Leach in his *Food Inspection and Analysis.*

The Pharmacopœial assay of oil of lemon is without doubt known to all pharmacists, chemists and analysts. In our hands, with careful manipulation and some degree of patience, it has given fair but not satisfactory results. We have found the end point very uncertain and we have always felt that the assay was extremely tedious, demanding much of the analyst's time and attention and frequently causing trouble and annoyance.

One of the chief sources of trouble is the sodium sulphite used in the analysis. During the course of some routine work we were much surprised to obtain results which could not be accounted for until we examined the reagent in question. Two analyses of the salt showed that it contained about *4 per cent. of sodium sulphite, instead of being chemically pure as the label stated.* The rest had, with amazing rapidity, been oxidized to the sulphate. We studied this matter a little more closely and found that another sample of sulphite, containing water of crystallization, which had been assayed in June, and found to comply with the U S. P. requirements, contained approximately 76 per cent. of $Na_2SO_37H_2O$ in September. Elvove in a previous number of this journal [6] has recorded a thorough investigation of this subject. Our only comment is that all sulphite should be roughly assayed by the U. S. P. method just before using and that an amount of salt should be taken, which contains the equivalent of 10 grams of anhydrous sodium sulphite or 20 gms. of sodium sulphite containing 7 molecules of water of crystallization for each 100 cubic centimetres of water used in making up the solution.

Another debatable point involves the amount of rosolic acid T. S. which is to be used in the assay. Our own experience has shown that the indicator should be added at intervals during the

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[4] *Chem. Druggist,* **74,** 81.
[5] *J. Ind. and Eng. Chem.,* **1,** 798.
[6] THIS JOURNAL, **82,** 211.

course of the analysis until further addition causes no marked pink color in either the control or the test, after heating for a reasonable length of time in a water bath which is boiling briskly. We have found it best to add the rosolic acid solution from a calibrated 1 c.c. pipette.

The end point is, as we have suggested, by no means sharp and brings a large personal error into play. After summing up the points of weakness of this assay, and adding to them the fact that Citronellal may be determined and reported as Citral, we reached the conclusion that, as a means of roughly approximating the true Citral content, the method was entirely too involved and laborious.

In trying to find a suitable substitute we have made some tests using the method outlined by Chace and also the one described by Hiltner.

Chace's fuchsin-sulphurous acid method was followed without great modification. (We found it convenient to use a refrigerator with a temperature of 13° to 13.5° C. and to make our comparisons at the end of 15 to 20 minutes.) For a description we refer the reader to Chace's original article or to Leach's *Food Inspection and Analysis,* page 866. Nessler tubes were used instead of a colorimeter, and varying amounts of a standard solution of pure Citral in aldehyde-free alcohol were employed for comparing color values. The method is rapid and gives results which are in general slightly higher than those given by the U. S. P. assay. Unfortunately this excellent and rapid method involves the use of aldehyde-free alcohol, a reagent which cannot be obtained in a short time. This handicaps the analyst who assays but few samples of the oil and who is called upon to report quickly. Under these circumstances he has little time to wait until the aldehyde has been removed. (We found that more than eight hours' boiling under reflux and that considerably more than 5 gms. of metaphenylene diamine hydrochloride were necessary to eliminate most of the aldehyde in 1000 c.c. of 95 per cent. grain alcohol. Even then our distillates gave a distinct aldehyde reaction.)

Hiltner's method with slight changes has, however, proven sufficiently satisfactory to warrant a brief outline of the procedure followed in this laboratory. A more detailed description may be obtained from the author's original paper.

A standard solution of Citral made by weighing accurately between 50 and 70 mgms. of pure Citral and making up to 50 c.c. with

alcohol was found satisfactory. Each cubic centimetre then approximates 1 mgm. of Citral. (100 to 130 mgms. in 50 c.c. may be used and smaller aliquot portions taken for the test.)

Ninety-five per cent. alcohol without previous purification was used in all the operations herein recorded. A 1 per cent. solution of metaphenylene diamine hydrochloride in diluted alcohol was employed as reagent. This solution was shaken with, and filtered through bone black before using.

About 1.5 c.c. of oil of lemon is measured into a 50 c.c. weighed flask, accurately weighed, and made up to the mark with 95 per cent. alcohol, stoppered and thoroughly shaken. From two to four c.c. of this solution are then accurately measured from a pipette calibrated to 1/100 c.c. into a Nessler tube, 10 c.c. of the filtered solution of metaphenylene diamine hydrochloride added, and the volume made up to the 25 c.c. mark on the tube, with alcohol. The same or a corresponding amount of standard Citral solution is then pipetted into another tube and treated in the same way. The solutions after shaking are compared by viewing them transversely and the stronger one is diluted with 95 per cent. alcohol until the reddish-yellow colors appear to be identical. The volumes are then measured and the subsequent calculations are based on the amount of Citral present in the standard. If these volumes vary more than 4 c.c., one from the other, the test should be repeated using a relatively smaller amount of the stronger solution. We have found it advisable to compare the colors of the solutions when approximately 3 to 5 mgms. of Citral are present in the standard. Two or three close readings, all of them made in volumes of approximately 25 c.c., should be obtained.

The method of calculating the results is comparatively simple. Taking as complex a case as possible:

Assume that each c.c. of the standard contains 1.2 mg. of Citral, and that there are 1.30 grams of lemon oil in 50 c.c. of an alcoholic solution. Then, if 3 c.c. of the standard and 3.2 c.c. of the solution of oil of lemon are used in the test—and if the *final* volume of the standard is 26 c.c. (after colorimetric comparison and dilution) and provided the other solution measures 25 c.c.—

Each c.c. of the *diluted standard is equivalent to each c.c. of the other solution,* and contains $\frac{1.2 \times 3}{26}$ mgs. of Citral.

The *total final* volume of the unknown (oil of lemon) solution

then contains $\left[\frac{1.2 \times 3}{26}\right] \times 25$ or 3.46 mgs. of Citral.

In other words 3.2 c.c. of the original solution of oil of lemon contain 3.46 mgs. of Citral and *3.2 c.c. of this same solution also contain 83.2 mgm. of* OIL $\left(\frac{1.300}{50} \times \frac{3.2}{1} \times \frac{100}{1} = 83.2\right)$

Then $\frac{3.46 \text{ mgm. Citral}}{83.2 \text{ mgm. of oil}} \times 100 =$ Percentage Citral in the oil $= 4.16$ per cent.

It may be of interest to note the close readings which can be obtained by the metaphenylene diamine method. They are shown in Table I.

TABLE I.

Sample number	Per cent. citral (Hiltner's Method)
IIa	3.88; 3.89.
IIb	4.19; 4.22; 4.07.
9469	4.05; 3.89.
9427	4.11; 4.11.

Table II shows the Citral content of the oils as determined by the three methods.

TABLE II.

Sample number	By U.S.P. Method	By Chace's Method	By Hiltner's Method
II	4.17 per cent. 4.44 per cent.	4.20 per cent.	4.16 per cent. 3.89 per cent.
9469	4.30 per cent.	4.50 per cent.	3.97 per cent.
9427	4.04 per cent.	4.35 per cent.	4.11 per cent.

As a result of this limited investigation, we beg to recommend that the Hiltner method be further studied, and that if possible, it be substituted for the pharmacopœial sulphite method now in use. The former is apparently more accurate (since it does not determine the Citronellal and thus introduce a positive error) and is undoubtedly much more rapid and far less troublesome. The results obtained may naturally be somewhat lower and if the method is adopted it may be found necessary to change the U. S. P. requirements from 4 per cent. to approximately 3.8 per cent. of Citral.

Research Department,

SCHIEFFELIN & Co., New York.

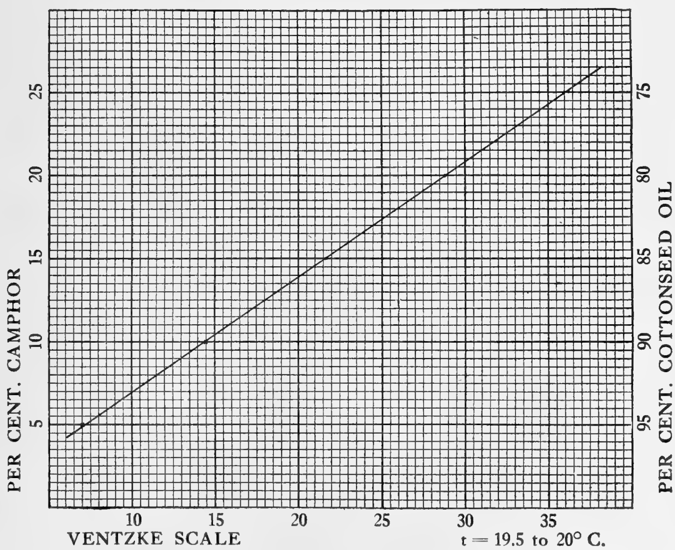
November 1, 1911.

FACTORY CONTROL OF CAMPHORATED OIL WITH THE AID OF THE SACCHARIMETER.

By Horace North,

Analyst with Lehn & Fink, New York.

The formula for camphor liniment official in the U. S. P. VIII requires that 200 gms. of coarsely powdered camphor be dissolved in 800 gms. of cottonseed oil. Solution is hastened by applying a gentle heat. By this process some of the camphor is volatilized, the loss varying with the degree of heat and the time necessary to effect solution, so that the finished preparation contains less than 20 per cent. of camphor. It is good policy, however, in order to



CAMPHORATED OIL

avoid disputes, for the manufacturer to furnish an oil containing fully 20 per cent. of camphor. The present article deals with a simple means for controlling the strength of the product.

Five solutions were prepared containing 5, 10, 15, 20 and 25 gms. of camphor, respectively, and sufficient cottonseed oil in each case to make 100 gms. Refined Japanese camphor of medicinal quality and high-grade cottonseed oil were employed. The camphor was granulated as finely as possible in a mortar. The ingredients were weighed into 300 c.c. Erlenmeyer flasks and the latter,

securely corked, were shaken at frequent intervals. By this procedure no camphor was lost and at the end of two days it was completely dissolved. Observations were then made in a Schmidt and Haensch saccharimeter. A 100 mm. tube was employed. The temperature during the readings varied from 19.5° to 20° C. The left field showed a reddish color which deepened with increased concentration of the camphor, so that, while the reading on the 5 per cent. solution was perfectly distinct, the observations became more difficult until with the 25 per cent. solution the precise reading was in doubt. Five to fifteen independent observations were made on each solution, according as the reading was more or less distinct. The averages on the five solutions were, respectively: + 7.0 + 14.5, + 21.7, + 28.9, + 36.2. With these data a graph was plotted.

In order, then, to examine lots manufactured in the laboratory, it is only necessary to fill a 100 mm. tube with the sample and observe the reading in the saccharimeter at or near 20°C. Reference to the graph indicates the percentage of camphor.

LIQUOR MAGNESII CITRATIS.

By M. D. Allen.

The manufacture and preservation of liquor magnesii citratis is a simple matter, yet one which gives the average retail druggist a great amount of trouble, as I have learned by experience.

The Pharmacopœial method, with which you are all familiar, gives an excellent product, if you can prepare it freshly as required, or if you can accurately gauge your demands for not over 24 or 36 hours. Either course is hardly practical, so that some method must be employed whereby the product can be preserved in good condition, for not only one day but several days, or weeks if desired.

I have used various methods without much success. The first which I tried was to dissolve the acid and magnesium carbonate in boiling water, filtering, adding the required amount of syrup and oil of lemon—for the flavor—and filling the bottles which had been thoroughly cleaned. I found, however, that at the end of about 24 hours a flocculent fungous growth would form and constantly increase. This method was then abandoned.

I next used the same process, but substituted the required amount of sugar, thinking that the fungus was in the prepared syrup. The results, however, were practically the same as before.

Later, I dissolved the acid in a small amount of water at a boiling temperature, added the magnesium carbonate and oil of lemon. After the reaction was completed the syrup was added and then a sufficient quantity of sterile water. The product was then heated to boiling and filtered. The bottles were previously prepared by boiling in a solution of sodium carbonate and thoroughly rinsed. These were then filled with the warm solution of citrate of magnesia. This product lasted nearly three days, but at the end of that period the fungus started to form just the same.

Next I tried adding a small amount of purified talcum, using the same process as the last mentioned. The product remained in good shape for nearly two weeks and it seemed that this would be the proper method, but precipitation began in that time and now after ten months you can see the results.

The next effort was to find out if the oil of lemon, which heretofore I had used directly was at fault. To get away from that, I made a flavoring tincture with enough alcohol to act as a preservative, but while this improved the flavor, it did not improve the keeping qualities.

The next effort was the one which seems so far to have been successful. The acid was dissolved in a small amount of hot water, then—previously mixed—the magnesia carbonate, sugar, purified talc, and flavoring tincture were added. When the reaction is completed add sufficient water and filter. The bottles were filled and closed. Then placed in an ordinary wash boiler, covered with water and boiled for about 30 minutes. Here is a sample treated in that manner, which has been on my shelf with no precautions as to care for five months, and yet it is as clear and effective as the day it was made.

I have also tried several sterilizations at 24-hour intervals, of the same lot, but find that one sterilization does the work as well as two or three, as can be seen by these samples which are plainly marked.

The excessive color I find is due to the frequency and the length of the sterilizations. This sample here is one taken from the regular stock, which is ready to have the potassium bicarbonate added and

be sent out to the customer. You will notice that there is much less color present than in the other samples.

℞,	Citric Acid	℥i
	Magnesium Carbonate	℥ss
	Flavoring Tincture	♏xxiv
	Sugar	℥ii
	Purified Talcum	grs. xlviii
	Aqua	qs.ad fl℥xii

U. S. P. Total Citric Acid	518 grs.	Difference 80 grs.
My Formulæ	438 "	
U. S. P. Magnesia	231 "	" 12 grs.
My Formulæ	219 "	

Flavoring Tincture consists of: Oil of Lemon, flℨ vi.; Oil of Orange flℨ iv; Tr. of Ginger flℨ vi; and Alcohol q.s. ad fl℥ iv.

PROGRESS IN PHARMACY.

A QUARTERLY REVIEW OF SOME OF THE MORE INTERESTING LITERATURE RELATING TO PHARMACY AND MATERIA MEDICA.

By M. I. Wilbert, Washington, D. C.

The tentative report of the Executive Committee of Revision on the scope of the U. S. P. IX has attracted considerable attention and has been liberally commented on both in medical as well as pharmaceutical journals. While it can hardly be expected that the individual substances agreed upon for admission to the coming edition of the U. S. P. will be endorsed by all, the comments that have appeared up to the present time have been quite favorable.

The Committee on National Formulary is calling renewed attention to some of the formulas that it is proposed to add to the forthcoming edition of the National Formulary. While all of the formulas have been published previously their systematic publication with the direct invitation for comment and criticism before final publication is being favorably commented on by editors of pharmaceutical journals and the resulting publicity should contribute materially to make the N. F. IV more nearly free from glaring errors of omission or commission than any of its predecessors.

The growing influence of the Council on Pharmacy and Chem-

istry of the American Medical Association on the progress of pharmacy in these United States is well illustrated by the nature and the importance of the references to the work of that Council as reported in the *Journal of the American Medical Association*. The American pharmacist who does not keep in touch with the progress of this work is missing an opportunity to prepare for the new pharmacy which is bound to result from the time and thought that is being devoted to materia medica and therapeutics by the leading minds in medicine today. The repeated evidence that there is need for efficient control of all important active medicaments will, in time at least, lead to the recognition that this control can best be exercised at the time of dispensing because no matter how efficient an article may have been when made, if deteriorated, it may be not alone worthless but even harmful.

No one agency, in this or any other country, is doing more to call attention to the need for the efficient control of medicines and the desirability of developing a thorough knowledge of the possibilities as well as the limitations of various drugs than is the Council on Pharmacy and Chemistry, and the details of the work referred to in the following pages will be found well worth studying at length in the original.

The American Druggist for many years issued twice a month, appears in October in an enlarged form with the announcement that in future it will be issued as a monthly.

New Yorker Deutscher Apotheker Verein.—This widely known and in many ways unique organization celebrated its Sixtieth Anniversary on September 28, 1911, under peculiarly pleasing circumstances. The "Kommers" held on that date was attended by one of its founders and now honorary president, the venerable Gustav Ramsperger, also by representatives of the medical as well as pharmaceutical professions who felicitated the organization on its long and honorable career.

N. A. R. D.—The thirteenth annual meeting of the National Association of Retail Druggists held at Niagara Falls on September 11 to 14, 1911, was well attended and unusually harmonious for an association which endeavors to safeguard the business interests of so large a number of members in different sections of the country. The financial condition of the Association is more satisfactory than at any period in its history, the Treasurer reporting the comfortable surplus of $14,000 in cash on hand.

The resolutions adopted cover a variety of subjects but are conservative and will go far to reinforce the Association in the place that it has established for itself. H. C. Shuptrine, of Savannah, Ga., was elected President, and Thomas H. Potts re-elected Secretary.

N. W. D. A.—The meeting of the National Wholesale Druggists' Association held in New York, October 10 to 13, 1911, appears to have been an unusually successful one both as to attendance and results. The address of President Schieffelin contained a powerful arraignment of the illegitimate sale of habit forming drugs and a plea for a national law to regulate interstate traffic in habit forming drugs.

Other features of the proceedings that are of interest to pharmacists at large are the reports of the several standing committees and the addresses by Dr. True and Prof. Remington. Dr. True reviewed the difficulties that have been met with in drug plant cultivation particularly of indigenous drugs, and called attention to some of the drugs that are being successfully cultivated in a larger way.

Prof. Remington presented an interesting report on the progress of the revision of the Pharmacopœia of the United States, the probable scope of the U. S. P. IX and the interest that is being evidenced in the revision generally.

HANBURY GOLD MEDAL.—The adjudicators of the Hanbury Fund have awarded the gold medal to M. Léger, a member of the Committee of Revision of the French Pharmacopœia whose work in connection with the active constituents of drugs has made him well known to chemists all over the world. —*Pharm. J. Lond.*, 1911, v. 87, p. 470.

DR. WILEY.—An editorial (*J. Am. M. Ass.*, 1911, v. 57, p. 905) in commenting on the charges against Dr. Wiley says: "When the charge against Dr. Wiley was first made public even his friends supposed that it could be at least sustained on a technicality. The investigation has brought out the fact that Dr. Wiley was not even guilty of the trivial technical violation that was claimed. The editorial also calls attention to some of the details brought out in the course of the investigation which are published in this and other issues of the *Journal of the A. M. A.*"

Another editorial (*Ibid.*, p. 1061) in calling attention to the decision reached by President Taft in the "Wiley case," says: "Dr.

Wiley's enemies are opposed to him because he represents a principle—that of protection to the consumer. They would be equally antagonistic to any other individual holding the same position and actuated by the same ideas."

U. S. P. Revision.—An editorial (*J. Am. M. Ass.*, 1911, v. 57, pp. 989-991) comments on the proposed scope of the U. S. P. IX and the relation of this first report of the Executive Committee of Revision to the practice of medicine. Measured by the guiding principle adopted by the present Committee of Revision, namely, that admission to or retention in the Pharmacopœia should be determined by "therapeutic usefulness or pharmaceutic necessity," the present report of the Committee of Revision is characterized as being disappointing. The editorial concludes that the one encouraging feature is that the tide appears to have turned and that the degeneration which Dr. Jacobi said was noticeable in recent revisions seems to have been checked, for a Pharmacopœia constructed on the lines foreshadowed by the first report of the Executive Committee of Revision is certainly a decided improvement over its immediate predecessor and should encourage physicians to renewed activity and interest.

Prescription Writing.—The editor of the Therapeutics column (*J. Am. M. Ass.*, 1911, v. 57, p. 1133) in an introduction to a series of articles on prescription writing presents a number of suggestions that should be of value to the pharmacist who is anxious to improve his prescription business, also discusses a number of questions that should be of interest to the pharmacist himself, from a professional point of view. Thus the following comment on the scope of the forthcoming Pharmacopœia of the U. S. P. is well worth considering:

"The proper use of drugs that have physiologic activities being acknowledged helpful and often curative, it is self-evident that we expect and demand a standard of strength and of purity of such drugs as laboratory and clinical determinations have proved valuable. Consequently we await the ninth revision of the United States Pharmacopœia with hope and faith that it will furnish the standards of useful drugs, and trust that it will not officialize and attempt to standardize drugs of no therapeutic value and of no 'pharmacal' necessity. A standard book that contains many useless articles insults its articles of value and loses them in a fog of uselessness."

Ethical Proprietaries.—M. E. Fussell, in a paper on the dangers of certain ethical proprietaries to both physicians and public, calls renewed attention to the fallacy of using ready-made mixtures, be they proprietary or official. He enumerates the misleading claims that are made in connection with a number of the more popular proprietary medicines and points out some of the dangers attending their use.—*J. Am. M. Ass.*, 1911, v. 57, pp. 1194–1198.

The Responsibilities of the Dispenser.—During recent months a number of articles in medical journals have called more or less direct attention to the responsibility of the pharmacist for the nature and purity of the medicaments dispensed by him on physicians' prescriptions. There can be no doubt but that members of the medical profession are devoting an increasing amount of thought to the problems that are involved and that pharmacists in the near future will be required to comply with the requirements naturally expected of them or submit to additional and possibly irksome restrictions in the conduct of their business.

Among the many subjects that have been recently discussed it will suffice to call attention to but a few, so as to point out the features to which attention should be directed in an effort to solve the problems now confronting American Pharmacy.

The Prescription from the Physician's Standpoint.—Dr. Thomas F. Reilly, in discussing this subject, expresses the opinion that the confidence of the medical profession in the integrity of the average pharmacist has been pretty generally shaken. He is afraid that until the pharmaceutical societies take the accusations that are being made against retail druggists in hand and punish without fear or favor the distrust now existing will grow.

He thinks it would be quite feasible for the representative medical societies to certify to the reliability of a number of pharmacists who are willing and able to supply medicaments of the required standard.—*American Medicine*, 1911, v. 17, pp. 528–532.

Lack of Drug Standardization.—Dr. Walter Eugene Hurley expresses the belief that the loss of confidence and the resulting indifference toward drug therapy has been brought about by the clinical failures seen every day by the average physician. He further asserts that the extent of variance from the requirements of the U. S. P. has been shown to be so great as to leave no doubt as to the unreliability of drugs dispensed in the routine way. He also

quotes extensively from the report of a recent investigation into the manner and accuracy of dispensing by New York City pharmacists, and points out that this report places a number of pharmacists in a very unpleasant light.—*American Medicine,* 1911, v. 17, pp. 541–543.

DIGEST OF COMMENTS.—A book review commenting on the uses of the Digest of Comments on the Pharmacopœia and the National Formulary points out that these bulletins serve to indicate the nature and the kind of remedies that are being used and actively discussed by physicians in different parts of the world. Not the least interesting of the truths that have been evidenced in this connection is the fact that the really active and efficient drugs are universally used by all classes of practitioners. It is also evident that the literature relating to the use of many of the less well established drugs is based on observations that are so unreliable or at least questionable that the mockery of their continuance as official articles must be apparent to every well trained medical man.—*J. Am. M. Ass.,* 1910, v. 57, p. 1398.

COMPARATIVE PURITY OF MEDICAMENTS.—Puckner and Warren, in reporting their examination of calcium phenolsulphonate, point out that the results of the examination of this substance further illustrate what other examinations in the Chemical Laboratory of the American Pharmaceutical Association have so often shown, and that is that commercial products which are but little used and for which there are no authoritative standards for strength and purity are also invariably unreliable in composition.—*J. Am. M. Ass.,* 1911, v. 57, p. 1384.

BRITISH PHARMACOPŒIA.—The Committee of Reference in Pharmacy has issued a further report containing suggestions for the revision of the British Pharmacopœia. This report is abstracted in the *Chemist and Druggist* (August 26, 1911, v. 79, pp. 354–358) and also commented editorially (*Ibid.,* pp. 351–352). The present installment includes many, if not all, of the changes that are involved in an attempt at compliance with the provisions of the Brussels Protocol, and it is gratifying to learn that with a limited number of minor exceptions and the recognized reservation that liquid preparations are to represent weight volume per cent., there is a general tendency to conform strictly with the requirements of the International Treaty.

The editor, in commenting on the revision of the Ph. Brit.,

points out that the reports as a whole are calculated to give pharmacists a very good idea of the progress of pharmacy within the last few years and by comparing the various recommendations and suggested monographs one will find little difficulty in constructing a skeleton of the new Pharmacopœia which, long overdue, should be published not later than 1912.

The *Pharmaceutical Journal* (London, 1911, v. 87, p. 296) in commenting on the third report made by the Committee of Reference in Pharmacy, says: "It is expected that the pharmaceutical and medical editors of the pharmacopœia will now undertake the preparation of a draft text for the consideration of the Pharmacopœia Committee. This work, it is said, will devolve upon Dr. Nestor Tirard and Prof. Greenish, and may be expected to occupy some considerable amount of time."

British Pharmaceutical Codex.—The new British Pharmaceutical Codex is now in press, and a sample monograph describing ergot and its preparations (*Pharm. J.*, London, 1911, v. 87, pp. 299–300) gives some indication of the extensive changes that have been made in the style and make up of the book.

Ash Content of Drugs.—John C. Umney, commenting on the paper on the ash content of drugs (Am. J. Pharm., 1911, v. 83, pp. 474–478) thinks that the author's deductions from the records he quotes are hardly justified. Umney believes that roots, barks and even leaves are capable of control by ash content and the matter of sampling offers no insurmountable difficulties in connection with drugs of high standard to be used as medicine.—*Brit. & Col. Drug.*, 1911, v. 60, pp. 342–343. See also editorial *Ibid.*, p. 339.

Acetylsalicylic Acid.—Seel and Friederich, in the first installment of a report on compressed tablets, present their result in connection with tablets of acetylsalicylic acid, and conclude that the commercial tablets are far from satisfactory and go far to account for the repeated complaints from physicians regarding the variable action of this drug.—*Pharm. Zentralh.*, 1911, v. 40, pp. 1055–1062.

Acetylsalicylic Acid.—A news note quotes from a report on the comparative prices of acetylsalicylic acid and aspirin in Paris and London. In France acetylsalicylic acid sells for about $1.33 per kilo (2.2046 pounds), while aspirin, which is a proprietary article, sells for $6.95 per kilo in 2 kilo lots or $10.13 per kilo in smaller lots.

In England the price of acetylsalicylic acid varies from 49 to 55 cents per pound. The name aspirin is still protected by registra-

tion. It sells at wholesale for $4.38 per pound and may be bought in single ounces at from 35 to 40 cents per pound.—*Oil, Paint, and Drug Reporter,* 1911, v. 80, Aug. 28, p. 37.

ADALIN.—Is brom-diethyl-acetylcarbamide prepared by the action of bromdiethyl acetyl bromide on urea. It occurs as an almost colorless and odorless crystalline powder with a melting point of 116° C. Adalin dissolves readily in alcohol and the other organic solvents. It is difficultly soluble in water. The product is said to be an efficient and prompt sedative, reducing excitement and promoting sleep in conditions in which a powerful hypnotic is not required.—*J. Am. M. Ass.,* 1910, v. 57, p. 1132.

BISMON.—Bismon is claimed to be a preparation of colloidal bismuth meta-hydroxide containing about 20 per cent. of metallic bismuth. Bismon occurs as a light brown granular substance forming with water fairly stable opalescent colloidal suspensions. It is said to have the action of other preparations of bismuth and is given in doses of 0.5 gm. in water.—*J. Am. M. Ass.,* 1911, v. 57, p. 1614.

BULGARA TABLETS, as described by the Council on Pharmacy and Chemistry, consist of the slowly dried cultures of Bacillus bulgaricus mixed with milk-sugar and starch, each tablet weighing 5 grains and containing a sufficient number of virile organisms to effect the souring of a pint of sterile milk in less than 20 hours.—*J. Am. M. Ass.,* 1911, v. 57, p. 1132.

CALCIUM HYPOPHOSPHITE.—Rupp and Kroll outline a titrimetric method for determining hypophosphorus acid in calcium hypophosphite by using the potassium bromate and bromide solution directed by the Ph. Germ. V for the determination of phenol.—*Archiv. d. Pharm.,* 1911, v. 249, pp. 493–497.

CALCIUM PHENOLSULPHONATE.—The Council on Pharmacy and Chemistry describes calcium phenolsulphonate as the neutral calcium salt of para phenolsulphonic acid. It occurs as a white or faintly pinkish white, almost odorless powder having an astringent, bitter taste. At high temperature the salt chars, emitting inflammable vapors having the odor of phenol and finally leaves a residue of calcium sulphate. Calcium phenolsulphonate is easily soluble in water and in alcohol.—*J. Am. M. Ass.,* 1911, v. 57, p. 1367.

CAPSICUM.—Harry E. Sindall reports a number of ash determinations on large lots of capsicum, and points out the impossibility of keeping the commercial product down to the limits given in Circular No, 19. This circular allows a total maximum ash content of

6.5 per cent. and 0.5 per cent. acid insoluble residue. Sindall thinks the standard should be raised to 7 per cent. total ash and 1 per cent. acid insoluble residue.—*J. Ind. and Eng. Chem.*, 1911, v. 3, pp. 753–754.

DIGITALIS AND ALLIED DRUGS.—Worth Hale reports a study of the effect of the digestive secretions on the activity of digitalis, digitoxin, digitalein and strophanthin. He concludes that while there is an appreciable deterioration of the several substances the rate of decomposition is such that it need not be taken into account in therapeutics.—*J. Am. M. Ass.*, 1911, v. 57, pp. 1515-1517.

EPINEPHRINE PREPARATIONS.—A report of the Council on Pharmacy and Chemistry points out the desirability of having a standard for epinephrine preparations recognized by manufacturers so as to insure uniformity of composition. The report outlines a method for assaying preparations of this type and suggests that the strength of epinephrine preparations be stated in terms of pure epinephrine and the strength of the preparations should not vary more than 15 per cent. from the strength claimed, when tested according to the method outlined in the report in comparison with a known quantity of pure epinephrine.—*J. Am. M. Ass.*, 1911, v. 57, pp. 1149–1150.

ERGOT.—Edmunds and Hale, in Bull. No. 76, Hyg. Lab., U. S. P. H. and M.-H. S., discuss the physiological standardization of ergot. They review much of the literature relating to the standardization of ergot, compare the several methods that have been suggested from time to time, report on a number of commercial products, and conclude that for practical purposes the cock's comb method is the preferable one at present. They also suggest that ergot preparations be marked with the date of manufacture, and that until more reliable methods of manufacture are found it would be wise to exclude all claims to permanency of ergot liquid preparations.

An editorial (*J. Am. M. Ass.*, 1911, v. 57, p. 1211) in commenting on the Bulletin by Edmunds and Hale points out that the primary object of the work was to test the comparative value of the several methods of assay. Incidentally, however, the results show that the available preparations of this drug are far from being uniformly reliable or fully satisfactory. Much of the deterioration noted is no doubt the result of aging. The editorial concludes with the suggestion that to insure uniformity in preparations of ergot and digitalis it may be desirable to have the U. S. Government

establish a system of continuous control similar to that which has proven so satisfactory in the case of antitoxins and vaccine virus.

ERSEOL is quinoline sulpho-salicylate, which forms well defined white prisms with an acid reaction, and is easily soluble in warm water. It is recommended as a remedy for rheumatism and similar troubles.—*Chem. and Drug.*, London, 1911, v. 79, p. 348.

FERRO-SAJODIN is described as basic ferric iodobehenate. It is said to contain about 5.7 per cent. of iron and about 25 per cent. of iodine. It occurs as a reddish brown powder unctuous to the touch. It is insoluble in water, soluble in chloroform and ether. Ferro-sajodin is said to have the action of iodides and of iron. It is claimed to be more stable and palatable than ferrous iodide and not to injure the teeth or disturb the gastrointestinal tract.—*J. Am. M. Ass.*, 1910, v. 57, p. 1132.

HELGOTAN, a bromo tannin methyleneamido-bromide, is recommended as a dusting powder of high antiseptic value.—*Chem. & Drug.*, London, 1911, v. 79, p. 348.

LANOLIN.—An editorial (*J. Am. M. Ass.*, 1911, v. 57, p. 906) points out that as long ago as 1902 a court decision established the fact that lanolin became a non-proprietary name when the patent on the product expired. To help remove the misapprehension that exists regarding the use of this word the Council on Pharmacy and Chemistry has decided to list it as a synonym for the official title.

The editor (*Pharm. Journ.*, London, 1911, v. 87, p. 401) in commenting on the proposed use of lanolin in N. N. R. as a synonym for adeps lanæ hydrosus points out that the word lanolin is not now protected in Great Britain and appears in the British Pharmaceutical Codex as a synonym for hydrous wool-fat.

MORPHINE.—Thorburn, A. D., discusses the estimation of morphine with phenyl-ethyl alcohol. The author believes the method to be a practical one and even the comparatively high price of the phenyl ethyl alcohol does not appear to him to be prohibitory. An aqueous solution of morphine is made alkaline and shaken with a mixture of phenyl-ethyl alcohol, which is then partially evaporated and titrated.—*J. Ind. and Eng. Chem.*, 1911, v. 3, pp. 754–756.

OPIUM.—An editorial (*Chem. & Drug.*, 1911, v. 79, p. 384) asserts that next to China the United States consumes more opium than any other country. The total imports into the United States, for the fiscal year ending June 30, 1911, are said to be 629,842 pounds, as compared with 449,239 pounds in the previous fiscal year. It

is generally believed that a large percentage of the drug sold in the United States is used either by persons who have acquired the drug habit or, to a minor degree, for smoking purposes.

PANKREON.—Tannin-pancreatin compound. A mixture containing the active tryptic, diastatic, and steatolytic ferments of the pancreas and about 8 per cent. of tannin. Pankreon is a dry, grayish, odorless powder of a slightly acidulous taste. It is soluble in alkaline liquids and practically in waters and acid liquids.—*J. Am. M. Ass.,* 1911, v. 57, p. 1455.

PEPSIN AND PANCREATIN IN SOLUTION.—A. Zimmerman reports a number of laboratory studies of combinations of pepsin and pancreatin and concludes that these ferments exercise no destructive action upon one another, and that with the proper degree of acidity they can be kept in the same solution permanently, the loss of activity noted by other observers having been due, entirely, to the reaction of the solution and to the degree of such reaction.—*J. Ind. and Eng. Chem.,* 1911, v. 3, pp. 750–753.

METALLIC PEROXIDES.—The Council on Pharmacy and Chemistry describes a number of metallic peroxides which are compounds in which the hydrogen of hydrogen peroxide has been replaced by metals and which are readily decomposed with liberation of hydrogen peroxide, or of oxygen in an active state. The commercial products are usually mixtures containing but a limited amount of real peroxide; for example, commercial "magnesium peroxide" contains but about 15 per cent. of magnesium peroxide, while commercial "sodium peroxide" contains about 75 per cent. of sodium peroxide.—*J. Am. M. Ass.,* 1911, v. 57, p. 1209.

QUININE TANNATE is described by the Council on Pharmacy and Chemistry as the tannate of the alkaloid quinine containing from 29 to 35 per cent. of quinine. Quinine tannate has the action of other salts of quinine, but on account of its insolubility its action is less certain than the more soluble quinine salts. The lack of bitterness renders it a useful preparation for administration to children.—*J. Am. M. Ass.,* 1911, v. 57, p. 1287.

An editorial (*Ibid.,* p. 1304) in commenting on the report on the commercially available quinine tannate, points out the need for physicians specifying the brand of quinine tannate desired or suggesting to the pharmacist that he secure for dispensing purposes a brand of quinine tannate that complies with the requirements outlined by the Council on Pharmacy and Chemistry.

Salvarsan.—A book review calls attention to a volume on salvarsan published by Messrs. Meister, Lucius and Brüning Limited, 51 St. Mary Axe, London, E. C., for free distribution. This volume of 155 pages in addition to comments on the chemistry and the testing of salvarsan contains pharmacological notes, a discussion of the dosage and a number of clinical reports with a review of the literature up to the present time.—*Pharm. J. Lond.*, 1911, v. 87, p. 341.

BOOK REVIEWS.

Allen's Commercial Organic Analysis. Volume v. Fourth edition. Entirely rewritten. Edited by W. A. Davis, London, and Samuel S. Sadtler, Philadelphia. Philadelphia: P. Blakiston's Sons & Co., 1012 Walnut Street, 1911. $5.00 net.

In the fifth volume of this work, we find a number of subjects treated which are of very great interest to pharmacists. The monograph on "Coloring Matters of Natural Origin" is the work of W. M. Gardner, Bradford, England. Here will be found very many facts relating to the properties, methods of assaying and the formative analytical examination of such important products as logwood, catechu, cutch, gambier, turmeric, gamboge, saffron, cudbear, alkanet, safflower, orchil, litmus, etc. There are two other equally interesting monographs on coloring substances, the one relating to the coal-tar dyes by Mr. W. P. Dreaper and Dr. E. Feilman, and the other to the "Dyestuffs of Groups 6 to 12" by Dr. J. T. Hewitt. These contain in very condensed form invaluable information which one interested in these subjects is likely to require almost daily. The chapter on the "Analysis of Coloring Materials," by Mr. Dreaper and Dr. Feilman, is particularly well done and will save the user of the book much time in looking up the original papers in the literature. Another chapter of great interest to pharmacists as well as food analysts is the one treating of "Coloring Matters in Food," by Mr. Albert F. Seeker. The monograph on "Tanneries" was written by Mr. W. P. Dreaper, and has been well done, although the subject is one of the most difficult for the analyst in practice. Finally there is a chapter on "Inks" by Mr. Percy H. Walker, of Washington. This is of the same high order of excellence as the other monographs.

It will well repay the pharmacist to have all of the volumes of

Allen's "Commercial Organic Analysis" in his laboratory. These words are not necessary to those who used these books for reference during their days at college or in the university. Books of this character should be on hand for immediate use when necessity arises. It is from the wise use of books that mortars and graduates become successful instruments in the solution of the perplexing problems that arise behind the prescription counter or in the laboratory.

An Introduction to Vegetable Physiology. By J. Reynolds Green, Fellow and Lecturer of Downing College, Cambridge. Third edition. Philadelphia: P. Blakiston's Sons & Co., 1012 Walnut Street. $3.00 net.

The first edition of Green's Physiology was published in June, 1900. The author's treatment of the subject was so happy and his style so clear, that in spite of the fact that there are several good books on plant physiology written by teachers in the United States, the work has been quite largely used here. Professor Green was at one time professor of botany to the Pharmaceutical Society of Great Britain, and is well known for his researches in plant physiology. In fact, many of his articles have been printed in the *Pharmaceutical Journal* of London and extensively reprinted in the drug journals of the United States.

Those of us who have used the volumes of the earlier editions are gratified to find that in the third edition we have in many particulars essentially a new book. The correlation of the internal structure of plants with their physiological needs is emphasized in the light of more recent morphological studies. Professor Green combats the idea expressed in certain quarters during the past few years, that many changes may go on in the protoplasm without involving any interchange of its substance. He holds this to be erroneous, for in all the reactions in which the protoplasm is concerned its own auto-decomposition and reconstruction are involved.

The book contains nearly 200 illustrations, mostly dealing with the inner structure of plants. The whole subject is one of such great interest and importance and the treatment is so admirable in Professor Green's book that students in pharmacy, as well as others, might well be encouraged to use it.

A MANUAL OF STRUCTURAL BOTANY. An Introductory Text-book for Students of Science and Pharmacy. By Henry H. Rusby, M.D., Professor of Materia Medica in the College of Pharmacy of the City of New York (Columbia University); Pharmacognosist of the United States Department of Agriculture; Member of the Committee for the Revision of the United States Pharmacopœia since 1890. Octavo, 248 pages, with 599 illustrations. Philadelphia and New York: Lea & Febiger, 1911. Cloth, $2.50 net.

From the prefatory note we understand that the present volume is the first of two companion volumes, the second of which will be devoted entirely to Commercial Pharmacognosy. For this reason the book has been designed as an introductory work to this subject, as well as to general botany. It has been planned to suit the needs of students of both general science and pharmacy. The elementary facts of plant-physiology have been considered in connection with the anatomy, but the subjects of vegetable histology and of microscopical methods and technique are omitted from this volume, its object being to teach the reader all that it is possible for him to do in the examination of drugs with the naked eye or with the pocket lens. With the exception of the last 25 pages, this volume of Dr. Rusby's work on "Structural Botany" reminds one very much of "The Structural Botany or Organography on the Basis of Morphology" of Prof. Asa Gray, published more than 30 years ago. The treatment of the subject is, however, quite different, Dr. Rusby considering the phytomer or phyton as the unit of structure. He regards the flower as a modified branch. Nearly one-half of the book is devoted to the study of the flower, including: Anthology, or its general nature; the laws of floral structure; the perigone; the andrœcium; the gynœcium; the torus and disc; dissection and analysis of flowers; and pollination and fertilization.

In the remaining chapters which deal with the structure of higher plants, we find a rather detailed and elaborate discussion of carpology or the functions and structure of the fruit, the seed, general structure of roots and stems, extension and appendages of the stem, the leaf and anthotaxy. There is a brief chapter on the cryptogams, and then follows a discussion upon botanical classification and analysis, botanical nomenclature and the collection and preservation of botanical specimens.

Dr. Rusby is well known for his studies in systematic botany, and as the author of a number of lengthy monographs on the Flora

of Bolivia. One might expect this book to embody the results of his critical study of plants in the field and herbarium during these many years.

Poliglota Vade-Mecum de. Internacia-Farmacio. By Celestin Rousseau. Paris: Librairie Hachette et Cie., 79, Boulevard Saint-Germain: 1911.

This book is quite novel, containing as it does, in readily accessible form, the comparative meaning of the terms used in defining and describing the substances included in the Pharmacopœias of nine different languages. It has been compiled with the hope that it will be useful to pharmacists of all countries and with the definite intention of facilitating the dispensing of medical prescriptions from abroad. It contains: 1. Comparative tables of formulæ of tinctures, extracts, pills, etc., in the different pharmacopœias. 2. The formulas of many preparations often prescribed in foreign countries. 3. A professional vocabulary in nine languages, which is arranged in such a manner that it can be used by any person who understands one of the following languages: English, German, French, Dutch, Italian, Spanish, Russian, Swedish or Esperanto. 4. General table of weights, measures, moneys, etc., of different countries. The work will no doubt be found very useful to pharmacists and physicians.

Chemical Analysis. By Prof. Frank X. Moerk. Published by the author. Philadelphia: 1911.

Professor Moerk, who is well-known to the members of the American Pharmaceutical Association for his papers dealing with the teaching of chemistry, the volumetric calculations of the U. S. P. (Proc. A. Ph. A., 1909), and classification of the quantitative statements of the U. S. P. (*Ibid.*, 1908), has recently published in two parts an outline of his laboratory courses in the Philadelphia College of Pharmacy. In Part I, "Course in Qualitative Analysis for Second-year Pharmacy Students" there is an excellent consideration of the groundwork required in the study of analytical chemistry. This study, as Professor Moerk states, "requires of the student the ability to write correctly the formulas of the substances used in the tests or experiments, which supplemented by the knowledge of a few general laws governing chemical changes, will enable the understanding of the reactions or changes taking place in the tests or experiments. This requisite fundamental knowledge consists in a

proper appreciation of the influence of the position of the elements in the electro-chemical series and the application of the valences of the atoms in the uniting of formulas of compound molecules, starting with the formula of binary molecules, and gradually leading up to the more complicated ternary molecules." These principles are clearly presented by Professor Moerk, and while we have numerous works dealing with the subject of qualitative analysis none is better adapted to needs of pharmacy students than the pamphlet in hand.

In the second part, entitled "Courses in Quantitative Analysis and Chemical Mathematics," attention is given to the methods for gravimetric determinations, volumetric determinations, gasometric determinations, organic analysis, alkaloidal assays, the determination of oils, fats and waxes, and the analysis of milk, vinegars and coloring matter. The portion dealing with "Chemical Mathematics" is a valuable part of the book.

A Pocket Medical Dictionary. By Dr. George M. Gould. Sixth edition, revised and enlarged. Philadelphia: P. Blakiston's Son & Co., 1012 Walnut St. 1911. $1.00 net.

This is probably one of the best, if not the best, book of its class. It is of very convenient size, and the definitions are very succinct and clear cut. The author is the prince of medical dictionary makers, and it is doubtful if Dr. Gould's work in this respect has ever been surpassed. The professional man needs dictionaries and the less space they take and the more convenient they are, the more they will be used and the less will one have the necessity of regretting the misuse or misspelling of words.

Books for Pharmacists, Edited by Harry B. Mason, Editor of the *Bulletin of Pharmacy,* Detroit, Michigan: E. G. Swift.

Three very interesting books have recently come from the press of *The Bulletin of Pharmacy*. They concern the retail druggist and should prove very suggestive to him. One of these is on "Window Displays for Druggists," the second edition of which has been recently published. This comprises for the most part, engravings and descriptions of over a hundred attractive displays which have been used with success by druggists throughout the United States. It also contains some useful suggestions on the subject of window dressing in general. While of course it is not expected that phar-

macists will use the forms which are here illustrated, yet the suggestions will no doubt be helpful in stimulating each one's individuality.

A second book from the same press was published during 1910 and is entitled "350 Dollar Ideas for Druggists." This is a compilation of articles for which pharmacists were paid at the rate of $1.00 each. In this are given hints on dispensing, manufacturing, advertising, bookkeeping and business methods. Here again is a symposium on mechanical devices, business methods and other subjects which pharmacists have found helpful in the conduct of their business.

The latest book of this series is entitled "Board Questions Answered." In this are given complete sets of examination questions used by different boards of pharmacy. Answers to these questions have been compiled by Mr. John Helfman, Assistant Editor of *The Bulletin of Pharmacy,* for the benefit of graduates of pharmacy and unregistered men who desire to review their knowledge preparatory to taking the board examinations. The object of this book is, as stated by Mr. Mason in his introduction, "on the one hand, to refresh the memory of students who have already taken an adequate course of pharmacy, and on the other hand to give them an idea of the type and character of questions asked by the different boards of pharmacy. There is no doubt that even the recent graduate in pharmacy needs some such special preparation. The writer well recalls his experience in going before two boards of pharmacy within a year after he had completed his college course. He found it absolutely necessary in both cases to spend two or three weeks in freshening up, so to speak, as well as familiarizing himself with the sort of questions customarily asked by the two boards. Without this preparation the chances are that though he was just out from college, he would have failed in one or both examinations."

"So well is this condition of things realized that in one of the leading University Schools of Pharmacy—a school having high ideals of scholarship—a special course on pharmacy board questions and answers is included in the last year's curriculum."

MODERN DRUG STANDARDIZATION. H. K. Mulford Co., 1911.

The present pamphlet has been prepared with the view of furnishing special information on physiological methods and standards. It contains a great deal of valuable information for pharmacists and

physicians. The physiological standardization of the heart tonics and heart depressants are considered in a very lucid and direct manner. The same thing may also be said with regard to the physiological standardization of cannabis indica, ergot, suprarenal gland and the thyroid gland. The references to the important published papers will be found useful to the practitioner or pharmacist who desires to look up the subject further.

The Pocket Medical Dictionary. Edited by W. A. Newman Dorland. Seventh edition, revised and enlarged. Philadelphia and London: W. B. Saunders & Co.

Dorland's pocket dictionary is of very convenient size for general use. The selection of words is fairly complete and the definitions are adequate for general use.

PHARMACEUTICAL MEETING.

The second Pharmaceutical Meeting of the course was held on the afternoon of November the 13th in the Museum of the College, President Howard B. French presiding. The first paper read was one by M. D. Allen, P.D., on "The Preparation of Solution of Citrate of Magnesia." He spoke of the various efforts that he had made to produce a satisfactory and permanent solution, one of which was by thoroughly cleansing the bottles with a solution of sodium carbonate. While some of these improved the solution, the fungus growth would ultimately come if the solution was kept on hand long enough. He now sterilizes the solution by placing the bottles containing the finished product in a common wash boiler, just covering them with water and then boiling for thirty minutes. His solution was a little weaker than the official in citric acid; he flavored it with oils of lemon, orange and tincture of ginger. Mr. W. E. Lee said that he had used sterilization for four years; he washed his bottles by the aid of sulphuric acid. Mr. W. L. Cliffe said that he believed in sterilization; he also said that if Mr. Allen did not follow the U. S. P. formula he should change his label and call it Allen's Solution of Citrate of Magnesia; such a label would comply with the law. Professor Kraemer spoke of the advantage of using a mixture of sulphuric acid, 1 pound, to four ounces of potassium dichromate in cleaning the bottles. Professor Lowe said he was interested in the discussion, especially on account of the author of the

paper having started his pharmaceutical career in his employ. He had practiced the sterilization of magnesium citrate solution for several years with most satisfactory results. In speaking of boilers, he said that it was better to use one composed entirely of tin, or of copper; a tin boiler with a copper bottom would not last so long, on account of galvanic action. President French gave some timely caution about following the law exactly, and the danger of taking advice to the contrary. He cited the case of a gentleman who had obtained the highest legal advice, even that of the Attorney-General of the United States, with reference to a business procedure which seemed somewhat at variance with the strict letter of the law. The advice was favorable to the enterprise and he acted accordingly, but later had the mortification of having a warrant issued by the government for his arrest for violation of the law. He also referred to the danger of copper poisoning in the use of copper vessels by the formation of verdigris.

C. Mahlon Kline then read a paper which contained some interesting comments on the Thirty-seventh Annual Meeting of the National Wholesale Druggists' Association. Professor C. B. Lowe spoke of the rapid deterioration of stillingia on keeping, also of buchu and the triangular gold signs put out by Helmbold in the 70's, on which was represented the gathering of the leaves by Hottentots from plants which looked like rushes; he also spoke of the high price of ginseng as being no criterion of its value, and of the care taken in India in the cultivation of cannabis indica. Professor Kraemer spoke about the increased cost of valuable indigenous drugs and that this price would ultimately have to be paid by the people. He also said that investigations were needed of nearly all plant drugs. Mr. J. W. England spoke approvingly of the work of the Bureau of Plant Industry at Washington; he also referred to the improvement of certain drugs by cultivation, notably, cinchona bark, and he thought that the standards might be improved by methods of cultivation. Mr. William E. Lee then read an interesting paper on "The Work of the Thirteenth Annual Convention of the N. A. R. D." After which several of those present referred in complimentary manner to the work of the association, and that of its efficient secretary, Thos. H. Potts. Professor Kraemer said that he wondered why the word "commercial" was so often used in referring to the work of the N. A. R. D., when as a matter of fact it is in many instances of the highest professional character as

seen in the U. S. P. and N. F. propaganda. A paper was read by Mr. J. W. England on "The Detection of Gum Ammoniacum and Gum Galbanum in Asafetida," prepared by Messrs. H. M. Seckler and M. Becker from the research department of Smith, Kline and French Company. The greatly increased cost of asafetida under the rulings of the "Pure Food and Drugs Law" had led to some adulteration by the above mentioned drugs. Various tests were given, one of the best being the production of volatile oils by steam distillation which would show a ten per cent. adulteration. Attention was called to the unique program issued by the German Apothecaries Society of New York, at the recent celebration of their sixtieth anniversary, also to some fine mounted specimens of flax presented by President French, one of the specimens being of American origin, one of Canadian, one of Argentine. The same card contained a specimen of the soy-bean plant, in fruit. After a vote of thanks to the authors of the papers read, and the referring of them to the publication committee, the meeting adjourned.

C. B. Lowe.

NOTES AND NEWS.

President French Portrait Fund.—Mr. Richard M. Shoemaker, treasurer of the Philadelphia College of Pharmacy, has sent in the following names of additional contributors to the President French Portrait Fund (see this Journal, pp. 237, 249 and 258):

Felicano Paterno, Santa Cruz, Manila.
James I. Scheffler, Pen Argyl, Penna.
J. C. Ladakis, Beirut, Syria, Turkey.
Guadalupe Morales, Granda, Nicaragua.
J. H. McCracken, Dinuba, California.
E. V. Howell, Chapel Hill, N. C.

Turin Exhibition Awards.—Messrs. Burroughs, Wellcome & Co. have secured no less than thirteen awards—eight grand prizes, two diplomas of honor, and three gold medals—for their exhibits at the Turin International Exhibition. This probably constitutes a world's record in awards received by a single firm at an exhibition open to all nations.

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TO VOLUME 83 OF THE AMERICAN JOURNAL OF PHARMACY.[1]

AUTHORS.

[1] Compiled by Florence Yaple.

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